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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN

HISTOLOGICAL CHANGES IN UTERINE MYOMATA IN THEIR TRANSFORMATION INTO FIBROID TUMORS.

By Ellis S. Allen, M.D., and C. C. Corson.

(From the McManes Laboratory of Pathology, University of Pennsylvania.)

During the past summer, together with a large number of other gynecological specimens sent by Dr. B. C. Hirst from his service in Howard Hospital in this city to the pathological laboratory of the University of Pennsylvania, there were about forty fibroid tumors of the uterus of varying size and situation in relation to the uterine wall. Of these thirty-six were examined by the writers, primarily for the purpose of description and record, and subsequently, after Dr. Brooke Anspach had kindly called our attention to the elastica changes in the uterine wall after involution from pregnancy, it was suggested that sections be also stained with a selective stain for the determination of the existence and distribution of elastic tissue as a possible structural constituent. Unfortunately from the mode of our work it has not been found convenient that we should prepare serial sections for direct and close comparison between the appearances given by the ordinary hæmatoxylin and eosin stain used originally in preparation and those afforded by the Weigert fuchsin and resorcin solution employed for the latter purpose.

The details of the histological findings in the individual specimens are reserved for future presentation with Dr. Hirst in connection with the clinical features of the various cases; but inasmuch as these tumors as a group have seemed suggestive of the series of changes taking place in uterine leiomyomata in their transformation into fibroid tumors, the features of this type are here brought forward separately. In this place the writers wish to express their thanks to Dr. Hirst for permitting such use of the material, and would also acknowledge the interest and assistance of Dr. Smith in their study of the specimens and in the preparation of this presentation.

In the examination of these tumors a single block of tissue was selected from each, preferably from the border, reaching into the mass of their growth; and it must be accepted that such selections, because of their small number and size, may not be truly representative of the entire growth in each instance, although in the entire group the error is not likely to be important. Sections from such blocks were originally stained with hæmatoxylin and eosin, and subsequently other sections from the same blocks, but not in known relation to the original ones, were stained with Weigert's elastica solution; in some instances new material had to be taken from the tumor mass, but always from the same place as the original block. Studied from such material but two of the tumors would merit the name of true uterine *fibromata*, if by this term it is understood that the growth is made up solely of fibrous tissue, and even these two examples exhibit a few scattered muscle spindles in the midst of the dense and finely fibrillar matrix. If one exclude from the class of true *leiomyomata* such growths as show at least a small presence of connective tissue distributed as investment of the muscle bundles, none of the tumors under examination could be ranked in this histioid group. The great majority of specimens examined by the writers in the present series show a preponderance of muscle elements in the structure, but with the added presence of a variably important amount of connective tissue which is seen distributed as an investment of the muscle and as an irregular framework in which the larger bloodvessels ramify, this tissue also being found now and again as practically the only constituent of small but definite nodular areas in this or that part of a growth. Of such tumors, usually spoken of as *fibromyomata*, the series included twenty-nine examples. Five were largely fibrous but showed a smaller admixture of muscle elements, perhaps meriting the combination name *myofibromata*.

The writers are inclined to look upon the original type of uterine myomata as represented by the larger subdivision of the group in hand. It seems impossible to exclude as proper to such growths the amount of connective tissue normal to the uterine wall as perivascular connective tissue or as intermuscular septa. Recognizing too that at least in the fairly formed bloodvessels walls there should develop some small amount of elastic tissue it would seem equally impossible to exclude such an occurrence from the unchanged myoma. From the analogy suggested by Anspach's[1] findings, that the vascular elastica is overgrown in the walls of uteri which have undergone involution after pregnancy, it cannot seem improbable that in the irregularities of development and life of

[1] Transactions of the Philadelphia Pathological Society, December 14, 1905.

a myoma at least here and there in the mass similar changes, with overgrowth of the vascular elastica and its extension about the vessel walls into the surrounding tissue, should take place. So, too, from its normal occurrence in the uterine wall, interlacing with the muscle in small amount, it would seem probable that it might in similar fashion be included in the growth of a myoma. In all of the examples of the tumors in the present series staining by Weigert's elastica stain has shown the presence of elastic tissue, ranging from its occurrence only in the vessel coats and in normal amount to such amounts as would almost justify the use of the term *elastoma* as part of the complete descriptive name of the new-

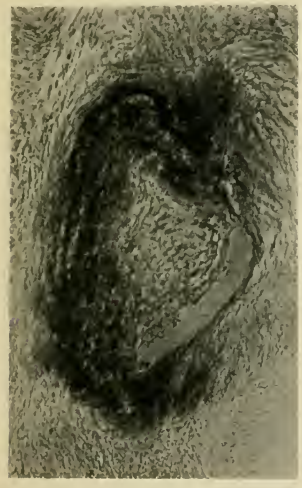

Fig. 1.—Obliterative endovasculitis with overgrowth of elastica (No. 620). (Zeiss 1/6; projection ocular; 30 cm. diam.)

growth. It has been more richly present in the nodular forms of the tumor, rather in the tissue between the nodules than in the latter themselves. It is found only in small amounts, if at all, in the general tissue of the dense fibrous areas of the combined type of fibromyoma, and is similarly absent in the rarer examples in the series of pure fibroma. Occurring in the midst of the tumor tissues as investments of the muscles, or in greater or smaller masses in the outer coats and outside the coats of the vessels, it has been found especially in those myomata which are apparently in process of change to become fibroids (including thus the greater number of specimens of the present series). In many of the vessels its occurrence is no greater in amount and not more irregular than would be regarded as normal. However, where there is evidence of vascular thickening or where obliterative changes are taking place in the vascular walls it is with uniformity found overgrown (Fig. 1), usually quite irregular and commonly extending from the vessel wall in greater or smaller amount into the surrounding fibromuscular tissues. In some cases dense masses irregularly extending along the course of some vessel are to be seen, from which smaller lines of the material are projected out into the muscle aiding in the investment of the muscle bundles (Fig. 2). Occasionally more compact bunches are seen about the vessel

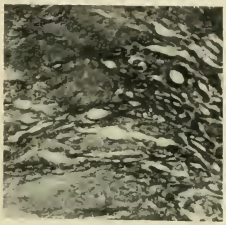

Fig. 2.—Showing elastica distributed in large amounts between the muscle. (Same magnification as Fig. 1.)

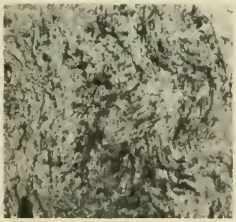

Fig. 3.—Showin gelastica in retrograde condition as coarse shreds and fibrils in midst of the fibroid tissue. (Same magnification as Fig. 1.)

walls, probably the same hyaline material referred to by Anspach. In a few instances the material, as it was seen in the fibromuscular substance of the tumor, was more or less broken, appearing as small lumps and fragmented threads (Fig. 3), the muscular tissue of such areas showing in more or less clear manner granular changes of the protoplasm with fine vacuolation and uncertainty of staining reaction, the fibrous fibrillæ of such places also showing more prominence than in areas or general sections in which such retrogressive appearances of muscle and elastica were absent. Finally, as far as this element is concerned, as above mentioned, in

the advanced areas of fibrosis and in the pure fibromata little or no elastica could be detected.

While it is impossible to declare positively as to the nature and mode of action of the cause underlying these changes, it seems not improbable that in a greater or less measure they are the result of nutritional disturbances connected with vascular changes of a chronic hyperplastic type; an idea which seems corroborated by the findings noted for these growths as far as relates to the bloodvessels and the appearances of the muscle and of the fibrillar material of which the fibroid areas are composed. In the present group the denser and more fibrous types have been tumors which, because of their position (as when almost isolated from the uterine wall beneath the peritoneum) or because of the density of encapsulation, would have suggested the idea that they had received a minimum of nutrition, their dense white tissue so completely as to be no longer recognized from the latter); and that there often exist evidences of faulty circulation in the occurrence of hemorrhagic foci and pigmentary deposits in the tissues (or occasionally in phagocytic cells) along their course. These dense areas, too, rarely present any number of cells such as can be considered antecedents of true fibrous tissues, fibroblastic elements being seen if at all rather in the less fibrous sections where more muscle persists, and then usually in quantities not suggesting the massive formations of fibroid structure commonly seen in advanced specimens and rather restricted to the walls and immediate neighborhood of the bloodvessels. Moreover, in these dense fibroid areas one commonly encounters a fine interfibrillar granular material which might be thought of as being in part at least a detritus rather than as wholly (as

Fig. 4.—Thickened wall of arteriole with hyaline change in its outer part. (No. 594, traced from a photomicrograph. Zeiss 1/12; projection ocular; 30 cm. diam.)

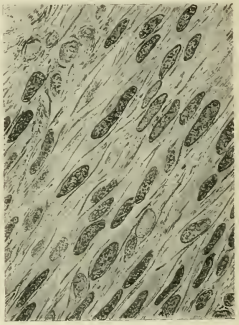

Fig. 5.—Undegenerated and non-fibrosed part of tumor (No. 594), showing large muscle cells. (Traced from photomicrograph. Zeiss 1/12 obj.; projection eyepiece; 30 cm. diam.)

tissue moreover indicating their relative avascularity. In comparing the bloodvessels of the various sections studied the occurrence of sclerotic thickenings, condensations, and hyaline changes (Fig. 4), which last apparently is in relation with an excessive amount of elastica, is most common in those instances where there are apparent a recession in amount of the muscle and a corresponding increase in the amount of the fibrillar tissue, this latter being in some measure composed of elastic elements. Further it is to be noted that the denser and more completely fibroid areas do not present vessels comparable in number with that of the vessels of the more muscular portions of such a growth; that their vessels are not conspicuous objects but more often appear as mere endothelial-lined channels in the midst of the fibrillar material (as if the outer parts of an original wall of the vessel may have merged and been lost in the surrounding usually interpreted) representing transverse sections of fibrils running opposite to the plane of section. That there is true fibrous-tissue formation cannot be doubted from the appearance of the vessel walls in the less dense portions of these growths, where the presence of fibroblasts and the outgrowths of elastic tissue are common along the outside of the vessels. It might thus be thought that in the evolution of a fibroid from a myoma that there occurs for unknown reason a hyperplastic process in the walls of the bloodvessels leading to an overgrowth of their fibrous elements and at the same time to an increase (in the manner indicated) of the elastic elements of their structure. Eventually, however, such changes occlude the affected vessels and interfere with the nutrition of the parts of the growth in which they are distributed, as an evidence of which perhaps stands the fragmented and altered appearance of this elastic tissue in

parts thus changing, and for which too the practical absence of such elastic tissue in permanently fibroid areas would argue. Close regard to the fibrillar material of these fibroid areas would indicate too that it presents features suggesting retrogression rather than active formation of true fibrous tissue, that while there are evidences of the true formation of fibrous elements along the course of bloodvessels at an earlier stage, these are insufficient to account for the massive fibroid changes frequently seen either locally in the tumor or affecting the whole tumor mass.

If such position be assumed there remains for consideration the part taken by the muscle of the original growth. Comparison of the various slides of the present series clearly indicates the fact (to have been expected, *a priori*) that the best preserved and developed muscle is to be found in those tumors in which the least vascular alteration is evident, or in those parts of a partially altered myoma where such vascular changes are

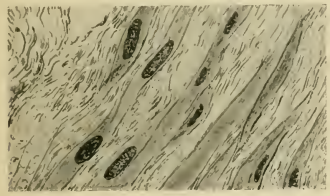

FIG. 6.—From same tumor as Fig. 5 (same magnification) but deeper in the growth; shows smaller size of muscle elements, distinct fibrosis, and in lower left corner muscle destroyed with persistence of fibrillar remnants.

least marked; and that coincident with the appearance of marked hyperplastic and sclerotic vascular changes and with the assumption of a fibroid character the muscle spindles are apt to show regressive changes of the character of simple atrophy of the cells and of degenerative and necrotic alterations (evinced by undue granularity of the protoplasm, shrinkage of the nuclei from an oval to a more and more slender rod shape, vacuolization of the protoplasm, and faults in the assumption of the stains). Eventually many or all of the muscle elements disappear and there remains behind a tissue whose character, while closely approaching the fibrous tissue of a scar, differs from the latter in the fineness of its fibrillation, in the absence of cellular elements or of the bellied shape of the fibrils, which would indicate their former cellular character, and by the presence of more or less fine interfibrillar granular material which may in part at least be of the nature of detritus. Often the remnant muscle elements of areas approaching this condition seem in direct continuity with this fibrillar material; and while such continuity of substance cannot be absolutely insisted upon, the idea that remnants of the muscle are contributing to the fibroid material is strongly suggested. Certainly no evidences of multiplication of muscle and formation of fibrous tissue from the products is shown in any of the specimens examined by us. The last portion of recognizable muscle constituent, aside from such fibrillar remnants, is the nucleus which is often seen isolated or still surrounded by a small amount of protoplasm embedded in the fibroid substance without any appearance of the features of multiplication, but commonly with evidences of retrogression in staining qualities, in size, and in the appearance of vacuoles in the nuclear plasm.

As illustrative of such muscular changes several photomicrographs (Figs. 5 and 6) are presented made from a large uterine fibroid, which having become parasitic upon

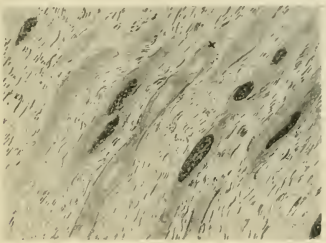

FIG. 7.—From same growth as in Figs. 5 and 6 (same magnification), but from deeper and more fibrillar part of tumor; shows few persisting muscle fibres in the midst of fine fibrillar stroma. Note absence of connective-tissue cells, degenerate condition of muscle (*x*) as well as the small size of these elements.

the lower border of the omentum, had become separated from its uterine attachment entirely and was thus suspended upon the omentum as a pedicle. Through some passive movement of the tumor the omental pedicle had been twisted in seven complete turns and presented an appearance not unlike the umbilical cord. The block of tissue from this growth was taken from the lower portion of the mass (at some distance from the omental attachment to the upper part of the tumor) and extended from the periphery for nearly 2 cm. into the interior. At the peripheral portion of the section (Fig. 5) the tissue is that of a nearly pure myoma, with large perfectly staining muscle spindles; in a slightly deeper portion (Fig. 6) the presence of a greater proportion of the fibroid material is shown, the muscle spindles are of distinctly smaller size, and at a point in the illustration (marked *x*) fault of staining and vacuolization of the muscle spindles are evident. In the next deeper portion the large

preponderance of fibrillar material is clear, and the apparent continuity of the evidently deteriorated muscle spindles with the fibrillæ of the general matrix is shown; the size of the spindles is materially smaller than in either of the more superficial levels, and isolated nuclei lie in the midst of the finely fibrillar matrix. In Fig. 4 is shown an arteriole with characteristic sclerotic thickening of its wall, a few fibroblasts and plasma cells lying just without the outer portion of the wall and the latter in a large portion of its circumference, merging into and practically indistinguishable from the surrounding fibroid matrix. Such a change or that represented in Fig. 1, where the lumen of the original arteriole is all but obliterated by a deforming endarteritis, represents the common types of vascular changes widely encountered in the specimens under examination and probably underlie the regressive changes of the tissue of the myoma which our observations suggest play an important part in the conversion of the tumor into the fibroid condition.

As a *résumé* of the above considerations the following may not be regarded as unjustified:

1. In uterine myomata there is always a certain amount of elastic tissue, either in normal amounts and relations in the bloodvessel walls or sometimes in the tumor tissue, where it is distributed among the bundles of muscle along with fibrous tissue of such septa and muscular investments.

2. Vascular changes of the type of fibrous and elastica hyperplasias are common in such tumors, leading to the thickening of their coats and eventual obliteration of the vessels, and increasing the connective-tissue framework of the tumor in the vicinity of the affected vessels.

3. Probably as a result of nutritive disturbances brought about by such vascular changes this excess of elastica in the surrounding tissues does not maintain an integral condition but deteriorates and eventually disappears.

4. Probably dependent upon the same nutritive disturbances the original muscular elements of the tumor also atrophy, degenerate and necrose, and finally disappear as muscle spindles, although there is some evidence that the cell wall (corresponding to the sarcolemma of the striated type of muscle) may remain and contribute in a passive manner to the fibrillar material of the final fibroid tissue. The character of the tissue and the relative paucity of fibre-forming young elements is consistent with the idea that the fibrillar tissue of the final uterine fibroid is in a large part not true fibrous connective tissue, and that the general process of transformation is not a progressive but a retrogressive one.

PRECOCIOUS DIAGNOSIS.[1]

By Edward Martin, M. D.,
Professor of Clinical Surgery, University of Pennsylvania; Surgeon to the Philadelphia and Howard Hospitals.

If twenty-five years ago it had been possible for the leading surgeon of Philadelphia to fall asleep and wake up today with no alteration in his faculties other than that incident to the refreshment of the prolonged rest, he would be profoundly impressed by the change in the character of the surgical material presented in a large clinic. He would look in vain for those huge, ulcerating, malignant growths which are still the delight of the book-maker, and for those gross lesions, the diagnosis of which is obvious across a public square. Not only would he see in the amphitheatre operations of which he had never heard, practised for the relief of conditions which were in his time unknown, but he would find other abnormal conditions habitually treated by the surgeon at a period in their progression when the physician of his time had not yet formulated the diagnosis. He would be astonished at the low mortality in formidable surgical procedures, which he would rightly attribute in the main to cleanly methods and the recognition of the rational treatment of shock and hemorrhage. He would, however, not fail to perceive that the low mortality is to a large extent dependent upon early intervention, special technique and individual skill playing a distinctly minor role.

Early intervention is, however, absolutely dependent upon timely diagnosis.

A competent diagnosis implies the complete picture of all the pathological conditions present. From the practical standpoint the mere naming of the lesion is of minor importance. Thus, if the humerus be completely broken in its middle third the diagnosis of the break is unmistakable and the condition is appropriately named. A failure to recognize associated nerve or bloodvessel injuries or the interposition of soft parts is a serious diagnostic error, since the sometimes irremediable effects of these secondary lesions may be prevented by immediate treatment.

[1] Read before the University Medical Society, January 19, 1906.

U. J. C. D.

From the surgeon's standpoint it is of cardinal importance that the diagnosis should be early. That it is not more often so must be attributed in part to the still prevalent method of preparing students for examination. They are taught the diagnostic features of the fully developed disease rather than those which characterize its beginning, and carry into their practical work the conception that the diagnosis need not be formulated till all the symptoms are present. Thus, if a student or practitioner of medicine be asked to give the diagnostic features of carcinoma of the breast, he will name the presence of a hard tumor, with retracted nipple, skin adhesions, and axillary lymphatic enlargements, in a woman near middle life or past it. It would save many lives if the students had thoroughly impressed upon them that the diagnosis should be based on finding in the breast tissues of an adult a non-inflammatory nodule or induration, which on removal is shown to exhibit the microscopic structure characteristic of malignancy. We should never see carcinoma of the breast presenting other diagnostic features than tumor. This end may be still further assured by rudimental teaching in the public schools, since delay in operating on these cases is usually due to worse than futile concealment on the part of the patient.

An important factor in the unsatisfactory position of surgical diagnosis lies in the lack of correlation in the work of the physician and the surgeon. Although it is true that the surgeon is at times appalled by the daring of his medical confrère, this manifestation of audacity is the exception rather than the rule, and is on his part usually an expression of willingness to take a desperate chance under nearly hopeless conditions. There are comparatively few physicians who habitually call in the surgeon in the early stages of affections, which persist in spite of conservative measures. Most cases of chronic bone inflammation or infiltration are treated medically for weeks or months, until local or constitutional symptoms, or both, show that the condition is other than rheumatism or neuritis. Gastric cancer rarely comes to operation before lymphatic enlargement has extended so wide as to make radical procedures impossible. Indeed, all intra-abdominal cancers are usually disseminated before they are seen by the surgeon. Huge empyemata are common in every large surgical clinic, and even the parietal malignant tumors are too often beyond reach before an attempt is made to cure them.

The evil effects of failure of co-operation upon the part of the medical man and the surgeon are in no way better illustrated than in the treatment of affections of the stomach.

It can be frankly admitted that a man busy with the mechanical part of his art is not competent to give an opinion upon the condition of the stomach. This requires both physical and laboratory examinations, the proper application nd interpretation of which need special training. Such examinations are essentially the functions of the internal medical man. It is true that even with thorough collaboration some unnecessary and futile operations will be performed, but with the doctor and the surgeon co-operating there will be a tendency toward conservatism rather than excessive zeal, and there will be fewer foolish gastroenterostomies for the relief of conditions secondary to cirrhosis of the liver, cardiac insufficiency, or chronic nephritis.

Since the requirement of today is that the diagnosis shall be made at a time when treatment may be serviceable, it will happen in many instances that such timely diagnosis can be formulated only by the aid of operation. This is particularly true in regard to intra-abdominal affections and invariably true of all malignant growths either intra-abdominal or extra-abdominal. The monetary cost at such exploration should be less than that appropriate to a major surgical operation requiring special skill and involving risk to life.

Perhaps, because these injuries are exceptional, birth traumata are usually overlooked till secondary irremediable changes have occurred. This is not so true of fractures and luxations as it is of the palsies incident to nerve lesion or cerebral hemorrhage. Each condition may call for prompt intervention.

From the surgeon's standpoint certain, rough, diagnostic rules can be laid down, too strict adherence to which, though it may lead to error, will more often suggest a timely diagnosis.

1. All apparently causeless, circumscribed, chronic, ulcers, persisting in spite of cleansing and protecting local treatment for more than two weeks, should be regarded as possibly syphilitic, tuberculous, or malignant. To this rule there are many exceptions, the majority of them obvious, such, for instance, as in the case of the varicose ulcers occurring about the malleoli. Where, however, there is reasonable doubt the diagnosis should be made promptly by the tuberculin injection, the administration test of mercury or mercury and iodides, or excision of a portion of the ulcerated surface and microscopic examination.

2. All non-inflammatory tumors of the breast should be regarded as probably malignant. The positive diagnosis should be made at once by excision and microscopic examination of a frozen section.

3. Pain and tenderness in the abdominal cavity if persistent or persistently recurring and sharply localized, if not accounted for by a recognized medical condition, and particularly if crippling in its recurring exacerbations, should suggest surgical operation. This is particularly the case if the pain and tenderness is associated with muscular rigidity.

4. Chronic diarrhœa characterized by small, fluid passages attended by some tenesmus; these symptoms being particu-

larly marked on rising in the morning, should suggest a rectal examination and a laboratory study of the stools.

5. Persistent, sharply localized pain and tenderness in a bone after trauma should suggest a fissured fracture; diagnosis to be confirmed or disproven by *x*-ray examination.

6. Persistent, severe, localized headache should suggest tuberculous, syphilitic, or malignant infiltration of the brain.

7. Persistent, apparently causeless, sharply localized pain and tenderness in either a bone or joint should suggest tuberculosis, syphilis, or, in the case of a bone, malignant infiltration.

It would, of course, be absurd to class every chronic joint affection as probably either syphilitic or tuberculous. The great majority are toxic or infective, but in every case of arthritis, except those acute in onset and course, the possibility of both tuberculosis and syphilis should be carefully considered.

From the practical standpoint we must accept the tuberculin test, the *x*-ray, and particularly the exploratory incision as the most helpful methods which have been recently introduced. It is difficult to overestimate the good effects which could accrue from the popularization with the profession of these methods, particularly were they supplemented by such an education of the layman as would result from an intelligently outlined public-school training on the symptomatology of the commoner diseases.

A STUDY OF TWO CASES OF SYRINGOMYELIA, WITH NECROPSY.

One with Subdural Cyst, Hydrocephalus, and Optic Nerve Degeneration.

By Henry S. Hutchinson.

(From the Ayer Clinical Laboratory of the Pennsylvania Hospital, and from the Department of Neurology and the Laboratory of Neuropathology of the University of Pennsylvania).

The pathological findings in the two following cases of syringomyelia offer a few features which may be of interest. Both cases are called syringomyelia, as each seems to present those essential features which are supposed to distinguish syringomyelic from other kinds of cavities in the cord.

Syringomyelia, as it is now conceived, is not a distinct pathological entity, and cases have lately been reported in which the authors seemed in doubt what term to apply to the process described. The essential feature seems to be the presence in the gray matter of the cord, usually posterior to the central canal, of one or more cavities, showing evidences of progressive development, and associated with glia-hyperplasia and with changes in the neighboring blood-vessels. Most authors include the glia-hyperplasia in their conceptions of the pathological process; in Schlesinger's definition of syringomyelia, however,[1] the glia-hyperplasia is merely "often present." A cavity caused by distention, of the central canal is sometimes known as a hydromyelia, but from many cases in the literature it would appear that the process leading to this distention is often identical with that, so far as it is understood, leading to a syringomyelia, and the latter name is applied by many to both kinds of cavities.

The first case is reported through the kindness of Dr. Morris J. Lewis, who will later publish a full account of the clinical findings, etc. The pathological material was very kindly given me by Dr. Warfield T. Longcope, who performed the autopsy.

[1] Die Syringomyelie, Vienna, 1902.

January, 1906. W. C., male, aged fifty years, white, married, childless. Contracted syphilis at age of twenty (1875), alopecia followed. Said to have been on "mixed treatment."

In 1890 he began to have headaches, and slight weakness in left leg, and shortly after this cerebral vomiting and transient tonic convulsions appeared.

These convulsions varied greatly in character, affecting either one side or other of the body, apparently indiscriminately, and were accompanied by unconsciousness. The first one seen (in 1890) was as follows: Arching backward of the head, dilatation of the pupils, turning of the head strongly to the left, with twitching of the *left* arm and leg, followed by transient paralysis of the muscles of the *right* side of the face, while another, occurring shortly afterward, affected the right arm and leg.

Choked disks were found, with hemorrhages into nerve head and retina with *complete, bilateral, temporal hemianopsia*. Sensation was blunted on the left side of the body. The knee-jerks were alike and normal. The urine contained no albumin. Under iodide of potash and mercury he rapidly improved, the convulsions vanished, and the choked disks, hemorrhages, and hemianopsia gradually disappeared. In one month's time the form fields had approached their

normal shape, although concentrically contracted, the left the more so.

Although the knee-jerks now showed exaggeration, he felt so well that he was able to go upon a hunting trip that required much walking and horseback riding.

Early in 1891, however, convulsions again made their appearance; these were epileptiform in nature, and were accompanied by an olfactory aura, and the left leg became more feeble. By autumn this leg became paretic, and he had a hemiplegic walk. It was now found that there was marked anæsthesia from the lower border of the ribs downward, and by the spring of 1892 there was almost complete anæsthesia from the nipple line downward, and control of the bladder and rectum was lost. During this whole period he had been taking iodide of potash, in large doses, daily. Complete paraplegia ensued.

A period of quiescence, lasting at least ten years, now came on, during which time he was able to be about in a wheel-chair and take pleasure in his surroundings in the country. He was not seen again until October, 1904, when he returned to Philadelphia, and almost immediately contracted typhoid fever, for which he was treated in the Pennsylvania Hospital. In consequence of his paraplegia, frightful bed-sores made their appearance. He recovered from the typhoid fever in about five weeks, but the bed-sores refused to heal, and he died a few weeks later, after returning to his home. During this period no change in the anæsthesia or paraplegia previously described could be detected.

The autopsy was performed by Dr. Longcope, June 24, 1905.

Anatomical Diagnosis. Compression of spinal cord in upper thoracic region, with subdural cyst; syringomyelia; moderate hydrocephalus; chronic leptomeningitis; chronic aortic endocarditis—two aortic leaflets; cardiac hypertrophy; chronic interstitial nephritis; acute bronchopneumonia; acute fibrinous pleurisy.

The body is emaciated, 178 cm. in length, with marked rigor mortis. Pupils equal. External genitalia apparently normal, Œdema of feet. Large, deep ulcer over sacrum and innominate bones.

Brain. The hardening fluid has affected the brain as the other tissues. Brain is of medium size. Dura not especially thickened; is not adherent to pia. Pia is whitish and more or less opaque, especially over the cortex, showing some general, rather streaky thickening. Convolutions well marked; sulci rather deep. Vessels at base show very slight thickening. The floor of the third ventricle bulges just below the optic chiasm. On section, the lateral ventricles are seen to be dilated, appearing several times the normal size. The right anterior horn is more distended than the left. On the left side the head of the caudate nucleus and the optic thalamus are well formed. On the right side the head of the caudate nucleus is much shrivelled, and the optic thalamus is also partially shrivelled. When a section is made through the upper part of the internal capsule on the right side an old cyst is found, occupying a large portion of the putamen of the lenticular nucleus, but extending also somewhat into the globus pallidus. The ependyma of the lateral ventricles looks thick and white. Several small cysts are seen in the choroid plexus of each lateral ventricle. The third ventricle is slightly dilated. The foramina of Monro (each) measure 7 mm. in diameter. The aqueduct of Sylvius is enlarged. Fourth ventricle is also large.

Spinal Cord. In upper thoracic region, before the dura is opened, there appears an enlargement. On cutting through the dura in the upper cervical region this membrane is seen to be quite thick, a little lower down it is found firmly adherent to the pia. The upper cervical region of the cord is fairly well preserved, but a little lower down the cord is seen to be somewhat flattened anteroposteriorly. Below the seventh cervical segment this flattening becomes very marked, and on the anterior aspect of the cord, where the dura is open, a definite cavity filled with fluid is found between the cord and the dura. The dura at this point is very thick. The eighth cervical and first thoracic segments, at least, seem to be intact, but small; immediately below this point the cord is seen to be compressed from the front, until it is converted into an indefinite, crescent-shaped mass of tissue a few millimetres across. The cyst-like formation in the membranes is open above, but ends below in a blind pouch, 11 cm. below the fourth cervical segment. Below the cyst the cord is surrounded by rather dense tissue, 1 cm. in thickness, which is limited by the dura. Section made here shows two open, longitudinal canals in the posterior funiculi, each measuring about 2 mm. in diameter. A section made 5 cm. below this point shows one large open canal, filling almost the entire cord. At this point no increase of tissue beneath the dura is seen. Traced downward, this large canal is seen to run for some distance in the cord, gradually becoming smaller, and disappearing before reaching the lumbar region. As it decreases in size it becomes surrounded by a narrow white line. At different levels in this cavity, delicate, cobweb-like threads are seen traversing it.

No gross lesions in the eyes or optic nerves.

Microscopically. The right pyramidal tract in the pons is a little degenerated. In the medulla oblongata the right pyramid is a little degenerated in its inner portion. The vessels in the pons and medulla oblongata are greatly dilated.

Sections through the middle of the cervical swelling (Fig. 1) show intense degeneration of the columns of Goll, slight rarefaction of the columns of Burdach, and considerable

degeneration in each lateral column, chiefly shown in the areas of the columns of Gowers and of the direct cerebellar tracts, but extending also far enough inward to implicate a considerable portion of the crossed pyramidal tracts. The degeneration of these latter tracts is evidently retrograde in character, as the sections examined are near the destroyed area of the cord. The sections here show a distinct central canal, with round lumen, lined by tall, epithelial cells. A

First thoracic segment: Section is very small as compared with a normal cord. The degeneration of the lateral columns is much the same as that described above in the cervical region, but is more intense. The dura is very thick; the pia only slightly thickened.

Upper thoracic region, just above the point where the cul-de-sac between the dura and the cord ceases (Fig. 2), shows that the cord is greatly compressed, completely

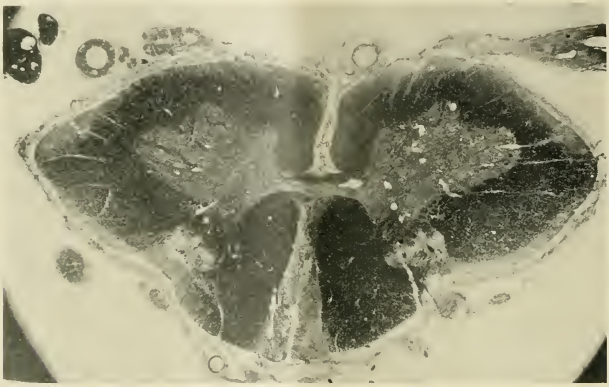

Fig. 1.—Case I. Cervical enlargement, showing retrograde atrophy of crossed pyramidal tracts.

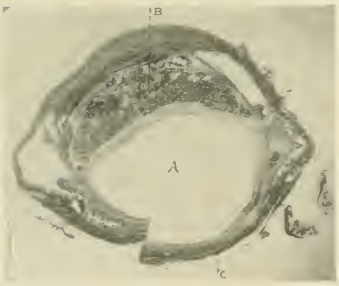

Fig. 2.—Upper thoracic region, showing subdural cyst (A), and, posterior to this, the necrotic cord (B). Anterior portion of greatly thickened dura at (C).

little lower in the cord no canal is seen, but a clump of epithelial cells appears. These transverse sections of the cord are smaller than normal.

degenerated, and much flattened anteroposteriorly; that the pia and dura are greatly thickened, and that between the dura and the cord is a mass of loose, fibrous tissue. The dura is seen to be made up of compact lamellæ of fibrous tissue; the thickened pia appears as strands of fibrous tissue, more loosely arranged than those in the dura. There is a large, oval, cyst-like space in the membranes anteriorly. The tissue forming the wall of this space is arranged in concentric, fibrous lamellæ. The nerve roots, cut in section, show much dilated bloodvessels, many of them with walls perfectly hyaline. No trace of central canal or ependymal cells seen.

Section at extreme lower end of the cul-de-sac (Fig. 3) shows that the cord at this level is not so compressed as in the section just described, but is as much degenerated. A small cavity, triangular in shape, is seen at the end of one posterior horn in the posterior columns, very near to the periphery. Between the dura and the cord, anteriorly, is seen a dense mass of fibrous tissue. A thick clump of cells occupies the site of the central canal.

A section a little lower in the thoracic region shows two distinct cavities, one occupying almost the whole of the

columns of Goll and Burdach and the posterior horn of one side; the other occupying the posterior horn, and extending into the lateral and posterior columns on each side of this horn. These cavities do not communicate with each other, the cavity described at the autopsy. Fig. 1 represents a section through the thoracic region a little below the level of that shown in Fig. 3. The normally stained nerve fibres are few, and chiefly gathered about the anterior horns and

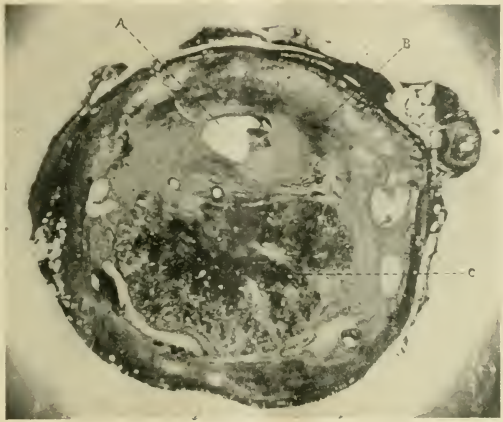

FIG. 3.—A few centimetres below section represented in Fig. 2. Extreme lower end of subdural cyst (A). Necrotic cord is shown at (C) surrounded by fibrous tissue (B).

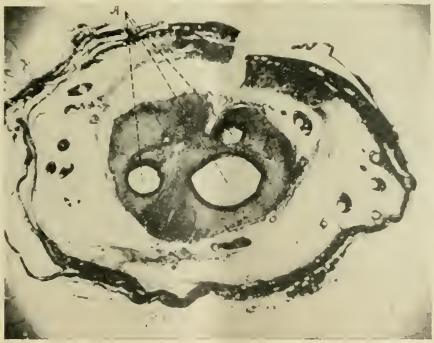

FIG. 4.—Slightly lower in the thoracic region. Cavities in the chord (A).

and, traced downward in the cord, each ends blindly. Each is replaced, however, by a new cavity in the corresponding posterior horn. One of these new cavities, traced downward, soon disappears; the other enlarges and forms in the posterior portion of the posterior columns. The fibrous tissue between dura and cord is not so dense as at a higher level. Serial sections were made through the lower end of one of the smaller cavities, and continued into the

beginning of the next cavity in the same horn; traced downward, the cavity gradually grows smaller, and, as it does so, is seen to be surrounded by a definite wall of thickened neuroglia. Before it has disappeared, a rarefaction of tissue in the gray matter just anterior to it can be seen. Traced downward this rarefaction becomes more marked, and finally gives place to a cavity. In the neighborhood of this cavity is a mass of thickened neuroglia. Each anterior horn, for a short distance, is also the seat of a small cavity, not surrounded by thickened neuroglia, and apparently the result of a rarefaction of tissue.

A little below this point only one cavity can be found (Fig. 5), and this occupies the whole of the anterior portion of the posterior columns, extending from one posterior column to the other, and greatly distorting the cord. The crossed pyramidal tract is degenerated on each side. This cavity, traced downward, grows smaller, and ceases in the lower thoracic region. Sections made immediately below the point where the cavity ceases, show, in the region corresponding to the cavity above, an area of glia-hyperplasia in which but few stained nerve-fibres are found. The

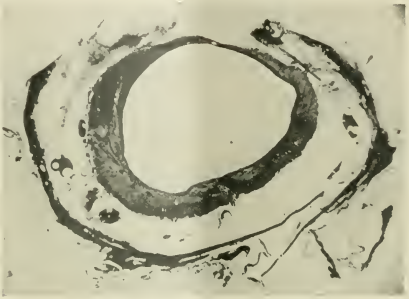

Fig. 5.—Middle thoracic region, showing a large cavity occupying most of the cord.

Fig. 6.—Lumbar enlargement, showing distention of subdural space, and retrograde atrophy (poorly shown) in the posterior columns. The crossed pyramidal tracts are degenerated.

thickening of the membranes, especially of the pia, is much less intense, and, where the cavity is very small, the pia shows only little clumps of thickened tissue, posteriorly and laterally.

Sections were made through one of the thread-like bits of tissue, which were described as passing from one side of the cavity to the other, traversing its lumen. Stains by fuchsin show a composite mass of fibres; stains by the Weigert hæmatoxylin method show a few black-stained nerve fibres, traversing the lumen of the cavity through the thread of tissue.

Below the point where the cavity ends, in the lower portion of the thoracic region and in the upper lumbar region, there is some sclerosis of the posterior columns (Fig. 6). This is evidently the result of a retrograde atrophy. The lumbar cord, except for secondary degeneration, seems to be normal. The subdural space is much larger than normal, and there was evidently an abnormal amount of cerebrospinal fluid about the lower portion of the cord.

A word about the walls of the cavities and the bloodvessels in the cord. Each cavity, where of good size, is seen to be surrounded by a layer of thickened neuroglia, arranged in strands of wavy lamellæ about the cavity. Toward the termination of one of the cavities, which was traced in serial sections, this lamellated appearance ceases; the wall of the cavity is here very irregular; necrotic tissue and even bloodvessels, transversely cut, project into the lumen.

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The bloodvessels throughout the cord appear greatly dilated, and show in the sections as large, round holes. All present thickening of their coats, and the walls of many are perfectly hyaline, staining evenly red (fuchsin). A few appear to possess no lumen, showing as circular, hyaline masses, staining red. From the outer coats of many, strands of connective tissue are seen streaming off into the surrounding nerve substance; where the vessels are cut in longitudinal section this is plainly seen. Sections stained by Van Gieson's and also by Mallory's connective-tissue method show these strands fading into the nervous tissue; small portions of the walls of the syringomyelic cavities are seen to be lined by wavy strands of connective tissue. The regions of the syringomyelic cavities show some increase in the number of bloodvessels.

Optic Tracts and Nerves. Microscopic Sections. The left optic tract appears to be normal. The right optic tract is not so wide as the left, and as it approaches the commissure is much degenerated on its inner aspect. The left optic nerve is very degenerated, and especially on its inner aspect near the chiasm (Fig. 7). The pia about the chiasm is somewhat thickened, and presents a very slight, round-cell infiltration. The right optic nerve (Fig. 8) is partially degenerated, especially in its central portion, but not so much as the left, and the fibres on the inner portion of the nerve do not appear to be more degenerated than those on the outer portion of the nerve.

Fig. 7.—Left optic nerve. Degenerated fibres in inner portion of nerve.

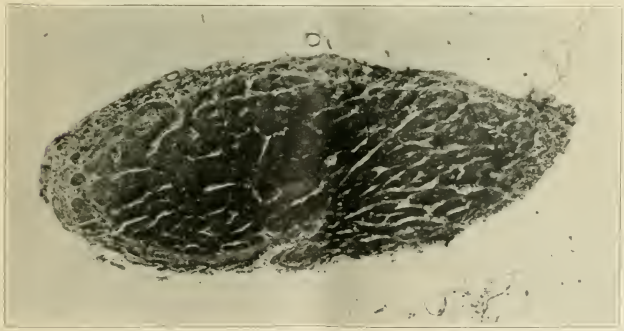

Fig. 8.—Right optic nerve. Some degeneration in centre of nerve.

The choroid plexuses of the lateral ventricles show, in the epithelium, a somewhat larger number of intracellular globules than normal. The bloodvessels are very dilated.

Microscopic examination of the other organs of the body confirms the anatomical diagnosis made at the autopsy. In addition, the liver shows advanced fatty degeneration.

For the pathological material of the next case I have to thank Dr. Charles S. Potts.

The case is as follows:

M. W., female, white, aged sixty-seven years, occupation cook. Entered Philadelphia Hospital in service of Dr. Burr, May 31, 1902. Hospital number, 698. Chief complaint "stroke." Family history: Father died suddenly, probably paralytic stroke; mother died of old age. Past medical history: had diseases of childhood; fourteen years ago had "stroke," and was in hospital two years and eight months. Was then able to walk only by using a chair. Present illness: had another "stroke" on the 24th of May, 1902, (one week ago); has been partially paralyzed on right side. Condition: woman past middle age, thin, and unable to walk. Pupils equal, and respond to light. Tongue-coated quite thickly and yellowish white. Pulse regular, but weak. Arteries comparatively normal. Considerable depression above and below the right clavicle; percussion note duller over right than over left apex. Heart negative. Reflexes present. Right knee-jerk apparently absent. Left leg somewhat deformed from an old fracture.

A year later, on June 13, 1903, 4.15 P.M. Patient dull, and so far gone that it is impossible to obtain any definite answers. Grip of right hand is poorer than grip of left. There is wasting of thenar and hypothenar eminences, and of the interossei muscles, equally marked in the two hands. The biceps, triceps, and wrist reflexes of the right upper extremity are prompter than those of the left. Has apparently no wasting of the lower extremities. Patellar jerk and Achilles jerk absent in both lower extremities, some movement in the quadriceps muscle of the right leg being seen, however. Plantar irritation produces extension of large toes on both sides. Tongue is protruded to about the lips. Left pupil is excentric. Both pupils respond slowly to light. The movements of both eyes are normal. Patient has apparently no anæsthesia. For the last three weeks has had incontinence of urine and feces. No paralysis of the muscles of the face.

Primary Diagnosis: Right hemiplegia.

Complications: Œdema of lungs.

Patient died June 13; time of day not given.

Microscopic Examination. Sections were cut at different levels in the cord and medulla oblongata.

The medulla oblongata is normal by the Weigert hæmatoxylin stain. The walls of the bloodvessels are somewhat thickened. There is moderate round-cell infiltration of the pia, and about some of the vessels in the medulla oblongata.

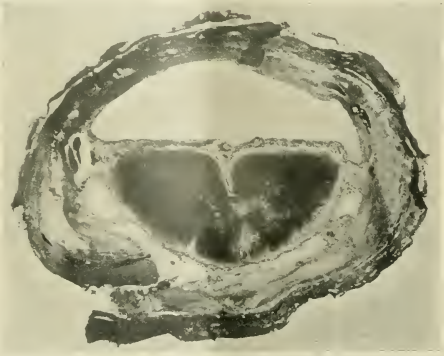

FIG. 9.—Case II. Upper thoracic region. Greatly thickened dura and adhesions between dura and cord. Rarefaction of posterior columns.

In the cervical region the posterior columns are much degenerated, as are also the direct cerebellar tracts. The dura and pia are thickened, and in the posterior part of the cord are firmly united. On the anterior portion the dura is still separated from the pia. There is degeneration in the peripheral zone of the anterior columns as well as in the lateral columns. A round-cell infiltration is seen in the pia, and the vessels of the pia are much thickened. In the place of a central canal there is seen a clump of cells, without lumen, passing over irregularly into the surrounding tissue. Lower down, in the thoracic region (Fig. 9), the degeneration in the posterior columns is intense, and the whole border zone of the anterolateral columns is much degenerated. In the posterior columns the nerve tissue

appears very rarefied, but in this tissue there are an extraordinarly large number of transversely cut bloodvessels, with thick walls. Adhesions between the dura and the pia are present at all parts, except in the anterior portions of the cord, and the dura is greatly thickened. At the site of the central canal there is the same clump of cells without lumen; but posterior to this, and separated from it by neuroglia tissue, is another similar clump of cells.

tinuity on either side, with a cleft extending into the posterior horns of the gray matter.

Still lower in the thoracic region (Fig. 11) the cavity is found to be larger, and to extend from the base of one anterior horn, across the posterior columns, to the posterior horn of the other side. The posterior columns and the border zone of the anterolateral columns are intensely degenerated. Some round-cell infiltration is found about

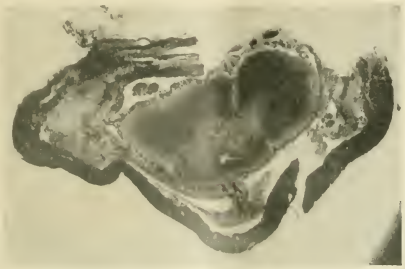

Fig. 10.—Lower than Fig. 9 Cavity seen in posterior columns.

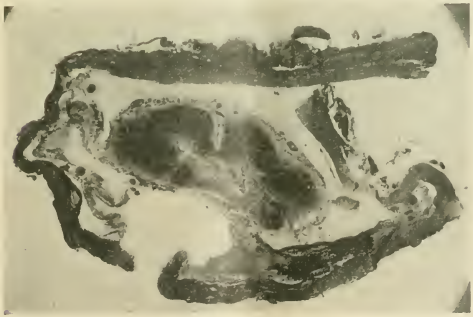

Fig. 11.—Slightly lower than Fig. 10. Notice great thickness of dura and adhesions to cord.

A little lower (Fig. 10) in the thoracic region the thickening of the dura and the adhesions between the dura and the pia are slightly less intense, but a cavity is found, star-shaped, in the degenerated posterior columns, and in each posterior horn of the gray matter there is some rarefaction of tissue. At the site of the central canal a group of cells is seen, the most posteriorly situated of which are arranged about an irregular lumen. Section taken a little below this point shows the cavity in the posterior columns now in contact the bloodvessels of the cord, and in the rarefied tissue surrounding the cavity. As in the sections above this point, the cavity presents distinctly the appearance of formation by rarefaction and absorption of tissue. The walls are very irregular, and bloodvessels project into the lumen, some of them appearing completely isolated in the cavity. About the cavity are many areas of homogeneous material, staining light pink (fuchsin). The cavity is nowhere lined by epithelial cells. The thickening and adhesions of the mem-

branes are less intense than higher up in the cord. The group of cells at the site of the central canal is divided into two parts, an anterior and a posterior, the latter having an irregular lumen.

At a little lower level in the thoracic region (Fig. 12) a cavity is seen, a short distance behind the site of the central canal, lined on its anterior and posterior aspects by epithelium. At its two lateral extremities the neighboring nervous tissue is markedly thinned out, and contains many thick-walled bloodvessels. As in Case I, strands of connective tissue are seen streaming off from the adventitia of the bloodvessels into the surrounding nerve tissue (Van Gieson's connective-tissue stain). The rarefaction of tissue in the posterior columns is no longer present, but this condition is now seen in the base of each posterior horn of the gray matter. The posterior roots are intensely degenerated; the anterior roots are more nearly normal. The thickening of the pia and dura is much less intense than higher up in the cord

and a left, separated by neuroglia tissue. Neither group possesses a lumen.

Résumé. Case I. Man, at age of twenty years (in 1875), contracted syphilis. Fifteen years later, headaches, vomiting, and convulsions appeared. The convulsions affected both sides of the body and were accompanied by unconsciousness. There was complete bilateral, temporal hemianopsia, and the ophthalmoscope revealed choked disks and retinal hemorrhages. Under anti-syphilitic treatment patient improved greatly, the convulsions left him, and sight returned. Less than a year later, however, the convulsions returned, and from the lower border of the ribs downward, first anæsthesia then paraplegia developed. For the next fourteen years, until the patient's death, there were no changes in the anæsthesia or paraplegia.

The anatomical findings were: In the upper thoracic region a large cyst in the membranes, anterior to the spinal cord, compressing and causing complete degeneration of the latter, and ending below in a cul-de-sac. Great

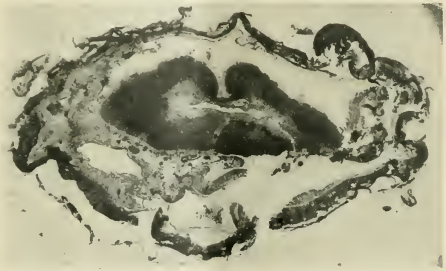

Fig. 12.—Thoracic region, lower than Fig. 11. Cavity in the gray matter.

Lower in the cord, but still in the thoracic region, the adhesion between the dura and the pia ceases, but there is still much degeneration of the posterior columns, the crossed pyramidal tracts, and the border zone of the anterolateral columns. No cavity in the cord is seen.

At about the twelfth thoracic level the degeneration of the cord is much the same as that described above, though less intense in all parts of the cord. The pia at this level is thickened, and very little infiltrated with round cells; the bloodvessels in the pia are thickened.

In the lumbar region the posterior columns are still partly degenerated, as are also the posterior roots. The anterolateral columns are no longer degenerated in the border zone, except near the posterior horns, where the area is occupied by the crossed pyramidal tracts. The ependymal cells of the central canal here appear in two groups, a right

thickening and adhesion of the membranes at and below this point. Lower in the cord, but confined to the thoracic region, several syringomyelic cavities of varying extent, one of them, the lowest, occupying the entire centre of the cord, having the cord about it as a narrow ring (Fig. 5). A moderate, internal hydrocephalus was present, and degenerations were found in the optic nerves, especially the left, and in the inner portion of the right optic tract. An old cyst was found in the corpus striatum of one side, and consequent degeneration of some of the pyramidal fibres below. The spinal cord, traced downward, showed more and more evidences of compression, until in the region of the cyst it appeared as a crescent-shaped, necrotic mass of tissue, surrounded by dense, fibrous tissue. Below this point it expanded again, to be occupied, however, by a series of cavities, the last and largest of these ending before the

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lumbar region was reached. These cavities, excepting a small one in each anterior horn, occupied the posterior horns of the gray matter. The lumbar region, except for retrograde degenerations in the posterior columns of the cord, appeared normal.

A distinct central canal was present in the upper cervical region, though it was surrounded by a dense mass of cells; below this point, throughout the cord, only a mass of cells without lumen, occupying the site of the central canal, were seen.

Case II. Woman came to hospital complaining of "stroke;" partially paralyzed on right side. Same kind of attack fourteen years before. Knee-jerk on right side absent; other reflexes, including pupillary, present. On day of death, a year later, knee-jerks on both sides absent, wasting of thenar and hypothenar eminences, and very weak grip in right hand. Eye movements normal, and no paralysis of facial muscles. Incontinence of urine and feces.

The anatomical findings were: A cavity of small extent, situated in the posterior half of the spinal cord, in the thoracic region. Above, this cavity appeared to originate in a rarefaction and absorption of the nerve tissue of the posterior columns; lower, where the cavity was somewhat more anteriorly situated, its anterior and posterior walls were seen to be lined by epithelium, while its two lateral extremities ended in thinned-out nervous tissue, rich in thick-walled bloodvessels. The membranes of the cord were greatly thickened, this being most marked at a level slightly above the cavity in the cord, where the membranes, posteriorly and laterally, were firmly adherent to one another. The pia showed some round-cell infiltration. The bloodvessels in the cord and membranes throughout showed thickened walls, and about some of them a slight round-cell infiltration was seen.

A possible connection between the several lesions in the first case suggests itself. The man had syphilis. This would account for the thickening and other pathological changes in the meninges. Where this process was most marked—in the upper thoracic region of the cord—all the meninges were found glued together. As a result of this, the spaces in the meninges above this point were no longer in communication with those below, and the flow of the cerebrospinal fluid was prevented. This fact would account for the cyst-like formation in the meninges, and for the great compression of the cord above this point. The prevention of the free circulation of the cerebrospinal fluid would cause a collection, under pressure, of the same in the cranium—over the surface of the brain and in the lateral ventricles. The consequent bulging of the floor of the third ventricle, with pressure on the optic tracts and chiasm, would account for the degenerations found in the optic tracts and optic nerves. That there was any direct connection between the pressure caused by the meningeal cyst in the thoracic region and the syringomyelic cavities found in the cord below this point is not likely. That one of these cavities, the largest, antedated the beginning of the cyst formation is very probable; the others may have originated later. As for the degenerations in the tracts, they were such as were to be expected from a complete destruction of the cord in the upper thoracic region.

The hydrocephalus, though its existence seems to be explained by the adhesions in the meninges of the cord below, may yet have some other explanation—in part, at least. Hinsdale[1] says that Kupferberg, in reviewing the literature, found out of 130 cases of syringomyelia, chronic idiopathic hydrocephalus present in fifteen. Couvelaire,[2] in

Fig. 13.—Normal optic chiasm, showing relation to third ventricle (A). Left optic tract at (B). It may be seen from this section how distention of the third ventricle exerts pressure upon the optic chiasm and optic tracts.

1899, reported a case of a man of thirty-six years, in whom there was great hydrocephalus and a cavity throughout the whole length of the cord; the cord was reduced to a mere shell. As for the degenerations in the optic nerves, these, as was remarked, are probably to be explained as a result of the hydrocephalus. Fig. 13 is a section through a normal optic chiasm, and shows the relations of the floor of the third ventricle to the chiasm. It will be seen from this that pressure may readily be exerted from the third ventricle upon the optic tracts and chiasm. The section was kindly lent to me by Dr. Spiller.

[1] Syringomyelia. Monograph. Philadelphia, 1897.
[2] Revue Neurologique, 1899.

Weisenburg and Thorington[1] have recently reported a case of syringomyelia with double optic neuritis, in which they believe the cause of the latter to have been internal hydrocephalus. They have been able to find, in the literature, only two cases of optic neuritis as a complication of syringomyelia, one by Bullard and Thomas, and the other by Saxer. Both of these cases showed at autopsy marked internal hydrocephalus. Weisenburg (*The Eye and the Nervous System: their Diagnostic Relations*, edited by Posey and Spiller) speaks of the possible connections between syringomyelia and optic neuritis, and emphasizes the importance of a complicating internal hydrocephalus. Referring to primary optic atrophy, he says that this occurs less often in syringomyelia (unless complicated with tabes dorsalis) than in any other disease. He also speaks of the as yet unexplained relation between optic-nerve atrophy and disease of the spinal cord, and, reviewing the theories put forth to account for this relation, he concludes with Gowers and others that the optic-nerve atrophy is uniformly progressive with the spinal-cord symptoms, and that both are due to the same primary cause—a lack of vital endurance, or an "abitrophy" (Gowers)—picking out especially the optic nerve and the spinal cord for degeneration. The involvement of the optic nerve in myelitis he explains in much the same way—by the action of a toxin which picks out, besides the spinal cord, especially the optic nerve. The optic nerves, in the first case, were not uniformly affected, the inner half of the left optic nerve and the inner portion of the right optic tract being completely degenerated. The cause of this could not have been general, but must have been local, and is found, probably, in the distention of the floor of the third ventricle. The other degenerations seen in the two optic nerves, especially those in the central part of the right nerve, may have their explanation in some such general cause as those mentioned above. That the pressure of the third ventricle upon the optic chiasm did not produce a permanent loss of function of the crossed fibres of the two optic nerves is shown by the fact that the left optic tract was found intact.

The retrograde atrophy of nerve fibres seen in the cord in Case I. deserves to be mentioned. In the cervical region the crossed pyramidal tracts, and in the lumbar region the posterior tracts, showed here and there degenerated, or rather atrophied, fibres. The nature of this process, in which the central stump of an injured or cut nerve fibre becomes atrophic, is not at all clear. Several explanations have been offered, but no one of them is satisfactory. The literature on this subject is not large. Spiller[2] in 1898 reported a case in which he found retrograde atrophy in the pyramidal fibres above, and in the fibres of the posterior columns below the seat of the lesion. He was able to trace this process for a distance of 4 cm. from the lesion. Recently J. R. Hunt[1] has published an article on "Retrograde Atrophy of the Pyramidal Tracts," in which he interprets the phenomenon as due to the functional inactivity of the motor cells. He says that the sensory tracts are comparatively free from this form of atrophy.

Mention was made of the fact that the epithelial cells of the choroid plexuses showed a somewhat larger number of intracellular globules than are normally found. Raubitschek[2] has recently studied the appearance of these globules and their occurrence in cases of meningitis. They give, as is known, the same reaction as fat with osmic acid, but can be differentiated from fat by special straining with pyronin. Petit and Girard[3] have found that they could experimentally produce a great increase in the number of these globules by administering muscarine and other drugs, causing, as they put it, a hypersecretion on the part of the cells of the choroid plexus. The occurrence in the present case of the globules in large numbers may be explained, perhaps, as the effect of some toxic substance in the blood or cerebrospinal fluid—possibly the same which caused the pathological changes in the meninges of the spinal cord, and, if their existence in numbers indicates a hypersecretion, they may stand in some relation to the hydrocephalus.

The mode of origin of the cavities found in the cords of these two cases is by no means clear. The etiology of syringomyelia is still somewhat obscure, and from the cases reported in the last few years, and from the work done on the subject, the causes of the lesion would seem to be very varied. In fact, nearly every writer on the subject has put forth some new view as to the possible origin of the disease in his case. From an examination of the different cavities found in the present two cases there would seem to be, in each case, certainly more than one process at work in the production of the cavities.

That most syringomyelias are congenital, or the result of some congenital malformation, is the view held by the majority of authors. Very many cases have undoubtedly this mode of origin: a faulty closure of the central canal in embryonic life, leaving, in the gray matter of the cord, posterior to the central canal, nests of epithelial cells which may later show a tendency to proliferate (Hoffman). But it is generally accepted that a typical syringomyelia may come into being in other ways than this. Vascular changes, especially hemorrhages; tumors—gliomata and sarcomata—reacting upon the surrounding tissue, and themselves degenerating; changes in the meninges, perhaps in relation with

[1] American Journal of the Medical Sciences, December, 1905.
[2] Johns Hopkins Bulletin, 1898.

[1] Journ. Nerv. and Ment. Disease, N. Y., 1904.
[2] Zeitschr. f. Heilkunde, April, 1905.
[3] Comptes Rendus, Soc. de Biologie, 1901, 1902.

vascular changes, and other processes have all been held to account for the presence of syringomyelia.

The congenital abnormalities may be small, and perhaps lie dormant in the cord until some exciting cause comes to start a pathological process. The cavities would then come into existence by the proliferation of the nests of epithelial cells about a previously existing lumen, with destruction of surrounding tissue, or by a liquefaction and absorption following an irregular proliferation of these cells. The epithelium of the central canal itself is believed to show sometimes an inherent tendency to proliferate, forming buds and shoots ("ependymal adenoma"—Babes). The exciting cause of the proliferation of these nests of cells or of the cells of the central canal would be direct or indirect—direct, if through toxins or otherwise the cells themselves were stimulated—and indirect, if, through destruction and rarefaction of surrounding tissue, the proliferation of the cells took place because of decreased tissue resistance.

As to the nature of this exciting cause, there are several opinions held. Schlesinger says that the cells being situated in the centre of the cord are in the position where vascular changes will be the most felt, and that in cases where the pathological changes in the bloodvessels are not quite sufficient to cause a necrosis of the tissue they may yet be sufficient to awaken in the abnormally situated cells a tendency to proliferate. Rarefaction of peri-ependymal tissue due to poor nutrition may, according to Redlich, give rise to a "hydromyelia." Saxer believes that the multiplication of the cells in question is a non-inflammatory, autochthonous cell proliferation, and that the later formation of cavities is due to vascular changes. Vetlesen[1] regards the proliferation as a species of genuine tumor-formation, with extremely slow development; according to his view, therefore, there would be a difference only of degree between this process and that which results in the formation of the large "sausage-shaped" tumors sometimes found in the cord.

Others have explained the glia hyperplasia in other ways: Some have defined it as a reactive inflammatory process, others have held that the process has its beginning in the proliferation of glia tissue which takes place in tracts of the white matter where the nerve fibres are degenerated. Nonne's[2] case is a good example of this last—where a large gliomatous mass in the centre of the cord seemed for some distance to be in direct communication with the degenerated posterior columns of a tabetic cord.

The role of the bloodvessels in the production of, or at least in the later development of, syringomyelic cavities seems a very important one. Much has been written lately on traumatic syringomyelia (Kienböck, Brasch, and others) and the production in the cord of cavities by extensive hemorrhages, the result of trauma. The rule used to be laid down that these cavities were to be distinguished from syringomyelia, chiefly clinically, in that the symptoms of the former were sudden, and of the latter chronically progressive (Van Gieson). Many claim, however, that the origin of a syringomyelic cavity may be in hemorrhages, at first small, later more extensive, therefore progressive. Spiller,[1] in 1896, reviewed the literature on this subject, and also spoke in favor of the probable origin of some syringomyelias in hemorrhages. These hemorrhages, he says, occupy usually the same portions of the gray matter of the cord chosen by syringomyelia, and often extend through a great length of the cord; as in the case of cerebral hemorrhages, they must become surrounded with somewhat thickened walls of neuroglia tissue. The reason that the gray matter is most frequently the seat of these small hemorrhages Spiller explains by the fact that it is much looser in structure, and more yielding than the white matter, the nerve fibres in it forming a reticulum, and not parallel columns, as in the white matter, and also because the gray matter is richer in vessels than the white. Kölpin,[2] reporting a case in 1905, says that he believes the cavity which he found, together with glia proliferation, has its origin in hemorrhages, at first very small, and gradually progressing; the effect of the first hemorrhages would be, by irritation of the surrounding tissue, to cause a reaction and proliferation of the same. As a result of this process, the bloodvessels themselves would be affected and a vicious cycle started. There was no history of trauma in this case, and the author believes the origin of the hemorrhages to have been either in the action of toxins or in a hemorrhagic diathesis on the part of the patient, and, from the fact that in his case the evidences of hemorrhages were seen in corresponding areas on both sides of the cord, he argues that perhaps certain sets of vessels have, in some persons, a predisposition to spontaneous hemorrhage. In Case II., above, the multiplication of the bloodvessels and the rarefaction of tissue appeared, it is true, in corresponding situations on both sides of the cord—namely, in the base of each posterior horn—and the cavity appeared to be growing only laterally and not anteroposteriorly.

Besides, by means of hemorrhages, the bloodvessels in the cord may cause destruction of tissue in other ways. Simple anæmia may cause rarefaction of tissue—ischæmic softening (Schlesinger). Or there may occur about the course of the bloodvessels a process of homogenization; later, liquefaction and absorption of the tissue, leaving cavities. This process of homogenization may be quite exten-

[1] Nord. Med. Ark., June, 1904.
[2] Archiv. f. Psychiatrie, Bd. xxiv.

[1] International Med. Mag., 1896.
[2] Arch. f. Psych., 1905.

sive, and perhaps accompanied by round-cell inflammation. Schwarz[1] reported such a case, and refused to call it a syringomyelia. Schlesinger remarks that this process occurring about the bloodvessels can hardly be held to account for the larger syringomyelic cavities. That stasis of the circulation, due to tumors or other cause, may give rise to cavity formation (Langhans) is a theory not generally accepted.

The importance of the connective tissue, which can be so often seen streaming off from the walls of the bloodvessels in the neighborhood of syringomyelic cavities, has been emphasized lately by Thomas and Hauser.[2] They found, as they show in a drawing, a cavity entirely lined by connective tissue, which latter seemed to be in direct continuity with the walls of a bloodvessel. The mechanism of the lesion, according to them, is: first, a multiplication of the bloodvessels with proliferation of their adventitia, and detachment of connective tissue from the same; these strands of growing connective tissue may isolate bits of nervous tissue, which will then disappear. Later there will be a disintegration of more substance, including the connective tissue itself, because of circulatory troubles. The proliferation of neuroglia they explain as a reaction against the invading strands of connective tissue. As to the nature of the original lesion —the multiplication of the bloodvessels—they are not able to pronounce on it, but they say that its cause is without doubt inflammatory. In Case I., above, the largest cavity was found lined here and there, for a very limited extent, by connective-tissue lamellæ, the strands of which were in places seen to be in continuity with the walls of bloodvessels. There was also seen in the neighborhood of each of the cavities in this case a large number of small, thick-walled bloodvessels. The strands of connective tissue streaming off from the bloodvessel walls seemed, however, to penetrate to no very great distance into the surrounding tissue, and it is hard to see how they could have been the cause of anything else than a possible inflammatory reaction in the neighborhood. Schlesinger, in his monograph, shows a drawing in which nearly the whole of a syringomyelic cavity is lined by connective tissue. This connective tissue, he says, remains after the nerve substance has softened and disappeared, and forms the "protecting innermost layer of the tissue limiting the cavity."

Cavities in the cord seem oftentimes dependent on changes in the meninges (Cases of Japha, Oppenheim, and others). As Schlesinger puts it, one of four things must take place: (1) the changes in the cord are primary; those in the meninges secondary; (2) vice versa, the changes in the cord are secondary to those in the meninges; (3) both groups of changes are co-ordinated; (4) their occurrence together is merely a chance combination. Saxer's case of acute cerebrospinal meningitis, showing at the autopsy great glia proliferation all through the cord, and cavity formation, is given by Schlesinger as an example of the second of these explanations; and Wieting's explanation of "meningomyelitis chronica," in which chronic meningitis is shown to affect not only the dura but also the pia and the cord, is accepted. In support of the third of the above explanations, namely, that the changes in cord and meningitis are co-related, Philippe and Oberthür[1] in 1899 reported a series of cases which seemed to show how syringomyelia and thickening of the membranes might be evolved together, under influence of the same cause, without being necessarily allied to one another. In their cases they found the greatest thickening and adhesions of the membranes (pachymeningitis symphysaire) at the level of the cervical swelling, and high up in the cervical regions, "regions most often showing the lesions of syringomyelia." In Case II., above, the thickening of the membranes was certainly most marked in the region of the cervical swelling, but here there was seen only a rarefaction of nervous tissue in the posterior part of the cord; the cavity was seen lower down in the cord, where there was distinctly less thickening of the membranes.

Nebelthau[2] has emphasized the importance of changes in the meninges, particularly syphilitic, in being the exciting cause in the production of cavities in the cord, and, speaking of syphilis, he remarks that in all cases of gliosis with cavity formation, in which the etiology is not clear, syphilis may be held responsible. By "not clear," he means not clearly due to congenital anomalies, to trauma with hemorrhage, or to inflammations of the meninges other than those syphilitic.

In Case II., above, where the cavity is comparatively small, it is easier to speculate on the possible origin and cause of the same than in Case I., where each cavity was fairly large. In Case II. the cavity was situated at a lower level in the cord than that at which the changes in the meninges were most marked; therefore the cavity was not solely dependent on these changes. The rarefaction of tissue and the presence of many small, thick-walled bloodvessels with round-cell infiltration at each lateral extremity of the cavity would point to some vascular disturbance as the cause here of the cavity formation, but anteriorly and posteriorly the cavity showed a wall lined by ependymal epithelium, with no rarefaction of neighboring tissue.

This lining epithelium was apparently in continuity above, where there was no cavity, with a clump of epithelial

[1] Zeitschr. f. klinische Med., 1898, Bd. xxxiv.
[2] Nouv. Icon. Salpêtrière, 17, 1902.

[1] Revue Neurol., 1899.
[2] Deutsche Zeitschr. f. Nervenheilkunde, 1900, Bd. xvi.

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cells separated from the central canal epithelium. Still higher, this clump of cells was seen to join the cells of the central canal. A possible explanation, in accord with Schlesinger's idea of the exciting cause of cell proliferation in such cases, would be that early in life, in the thoracic region of the cord, there existed, as the result of a congenital malformation, a nest of cells, with or without lumen, situated at some distance posterior to the central canal. Where these cells were farthest from the central canal, there the abnormal conditions in the cord must have been greatest, and the cord itself, therefore, most liable to suffer from pathological influence. When the thickening of the membranes and the vascular changes began the whole cord was affected, but though this thickening was greatest in the cervical region, the thoracic region of the cord, being congenitally the weakest, was most affected. The nest of cells there situated proceeded to proliferate. The vascular and meningeal changes, growing more marked, were then sufficient not only to arouse the process of proliferation in the abnormally situated cells, but also to cause those areas of markedly rarefied tissue which were seen in the posterior horns and in the posterior columns.

In Case I. all the cavities, excepting those in the anterior horns, had walls of thickened neuroglia, and none were lined by epithelium.

The opportunities for offering explanations of the origin of syringomyelic cavities are very abundant. Different authors have emphasized different points in regard to the etiology —the vascular changes, the changes in the meninges, the ependymal tendency to proliferate—and so forth, but each of these changes is generally recognized as having its own part to play, sometimes more, sometimes less important, in the production and extension of syringomyelic cavities.

The photographs are from sections stained by the Weigert hæmatoxylin method.

In conclusion, I wish to express my thanks to Dr. Spiller, under whose direction this work was done, for his kindness in giving me much help, and many suggestions.

REPORT OF A CASE OF HYSTERIA SIMULATING FRACTURE OF THE SPINE.

By F. H. Klaer, M.D.

It is well known that hysteria may simulate many forms of organic nervous disease, but a case that has recently come under our observation has offered unusual difficulties in diagnosis. The question of operation had to be considered, and it was therefore of much importance to determine whether the grave symptoms were the result of an injury to the spinal cord or of hysteria. The history of the case was as follows:

J. U., male, aged twenty-six years, single, was admitted to Dr. Charles H. Frazier's service, in the surgical ward of the University Hospital, at 7 P.M., September 18, 1905, having been injured the same afternoon at 2 o'clock.

Personal and Previous Medical History. He was born in Wilmington, Del. His early life was uneventful. He had had very little education. For several years he was employed in a shipyard. For the past six years he has been a brakeman on the railroad. He uses tobacco in moderation, but no alcohol, and denies venereal infection. About five years ago, in a railroad accident, he sustained a fracture of the right leg just below the knee, and fractures of two ribs on the right side. With this exception he has always enjoyed good health.

Family History. Unimportant, and not bearing on the case.

History of Present Condition. While standing between two tracks at a railroad crossing at Coatesville, Pa., he said he was struck in the back by the cross-beam of the tender of an engine, and knocked down between the tracks. At the same time another train was passing in the opposite direction, on the other track. For some time after he was struck he was unable to speak, though he never lost consciousness. He could move his legs, and sensation, according to his own statement, was preserved. He had, however, most severe pain in his back, and this was increased by the slightest movement of his body. He was carried to the station, later brought to Philadelphia, and admitted to the Hospital at 7 P.M.

On admission, September 18, 7 P.M., he was very nervous and excited. If left alone he lay slightly turned on his left side, maintaining this position by holding on to the head of the bed with his hands.

The abdomen was apparently very tender, and very rigid all over. Pressure anywhere over the body elicited expressions of severe pain, and caused him to toss his head and arms about and to grind his teeth. There was a slight depression of the ninth thoracic spinous process, the skin over this being unchanged in appearance though extremely painful and tender; there seemed to be slight movement here on turning the shoulders. He was able to lift the heels

about eight inches from the bed, and sensation was preserved in both legs, though it was somewhat dulled. (This part of the examination was unsatisfactory on account of the nervous condition of the patient.)

Examination four hours after admission revealed complete paralysis in both legs and loss of sensation in legs and lower part of body; the exact limits not determined.

September 19th. Patient's condition remains unchanged. He is very restless and complains of pain in his back, and refuses to eat. Paralysis of lower limbs and loss of sensation up to costal margin remain complete. Retention of urine and feces is present. The abdomen is still rigid and very tender to palpation. He is transferred to an air mattress.

20th. He is resting more easily. Repeated *x*-ray examinations fail to locate the seat of injury. The twelfth rib on the right side seems to be shattered near its connection with the spine. He has to be catheterized, and the bowels are moved by enema.

Examination by Dr. W. G. Spiller. The patient cannot move the right toes at all. He flexes the right foot very slightly at the ankle and can flex the left toes very little, but cannot flex the left foot at the ankle. He cannot move either lower limb at the knee, but can rotate either thigh at the hip very slightly.

Sensations for touch and pain are entirely lost in the lower limbs and over the abdomen and thorax to about one and one-half inches below the nipples. From this point to a little above the nipples sensation varies, and the line of anæsthesia gradually rises as the examination is continued. The cremaster reflex is prompt on each side. The patellar and Achilles tendon reflexes are entirely lost on each side. The Babinski reflex is absent on each side, there being a very slight response in flexion of the toes on each side. Sticking the sole of either foot with a pin causes a contraction of either thigh.

21st. The patient is able to move the toes of either foot and slightly to lift either knee from the bed, the power being better in the right leg. Tactile sensation has returned in the right leg, from the toes to the groin; also slight sensation is felt in the left foot, and to a point three inches above the malleoli. The slight depression at the ninth dorsal spinous process still persists, and over this the skin is unchanged in appearance. The slightest pressure gives exquisite pain, but no crepitus can be made out.

22d. Improvement in motion and sensation continues. The patient is now able to turn bimself in bed with the help of his hands, and voids urine voluntarily.

23d. Examined by Dr. Spiller. The patient has almost complete return of motion and sensation, and is able to turn over in bed, to sit up, and, with some assistance, after a little persuasion, to get out of bed and walk. On careful questioning it is now learned that, on the morning of the accident, in a quarrel with his landlord the latter had threatened to shoot him. The patient states that he had been worried about this and was not in his normal condition the rest of the day.

26th. He was discharged cured.

If we review the chief features of this report, the difficulties of diagnosis and the reasons for calling the case one of hysteria become apparent. A young man, naturally of a nervous temperament, was brought to the hospital with almost complete paralysis of his lower limbs, and loss of sensation in the lower limbs and in the trunk, almost to the nipples, and with the history of a severe railroad accident. The *x*-ray examination seemed to show a fracture of the right twelfth rib, but this was by no means positive; the slightest movement caused severe pain in the back; the abdomen was very rigid and tender; the ninth thoracic vertebra seemed to be slightly depressed; the bowels and bladder did not functionate normally, and the patellar and Achilles tendon reflexes were lost on each side. It is not surprising, therefore, that the case was at first regarded as one of fracture of the spinal column, but careful study at once revealed an hysterical element.

The man's life had been threatened the morning of the supposed accident, and by this he had been much excited. He had been employed during six years on the railroad, and had probably both seen and heard of many railroad accidents —in fact, he had himself met with an accident five years before, in a collision, in which his right leg had been fractured. He was therefore probably prepared for serious results following the blow from the train. Close questioning, moreover, caused him to modify some of his statements concerning the details of the accident.

The loss of speech for some time after the blow, although he was not unconscious, was suggestive of hysteria. Loss of voluntary power and of sensation did not occur immediately after the injury, but these signs developed shortly after his admission to the hospital, and after his attention had been drawn to them by the examination and the discussion of them by the attending physicians, and so could be suggestive of hysteria, as was also his excited condition at the time of, and after, his admission. Retention of urine and feces during two or three days was suggestive of organic disease, but its disappearance within so short a time was more suggestive of hysteria. Dr. Spiller found a very interesting condition of anæsthesia. The loss of sensation when the examination began extended over the trunk as high as one and a-half inches below the nipples, but repeated examinations caused the anæsthetic area to ascend, until at the completion of the examination it had extended almost as high as the clavicles. This was clearly an hysterical manifestation, and Dr. Spiller was therefore able to say positively, at his first examination,

that much of the symptom-complex was due to hysteria. The high level of the anæsthetic area did not conform to an injury low in the spinal column, as indicated by the deformity of the right twelfth rib and slight depression of the ninth thoracic vertebra. To explain this high level of anæsthesia on an organic basis there must have been a lesion of the cervical cord, but this could not have been possible with the perfect control of the upper limbs which existed in this case. The loss of the patellar and Achilles tendon reflexes was very suggestive of organic disease, but it may have been due to failure of relaxation of the muscles. The absence of the Babinski reflex, with the practically complete paralysis of the lower limbs, pointed to an hysterical origin.

If the slight depression of the ninth thoracic vertebra had been of recent origin, and caused by a severe blow, as the history indicated, one might expect to find some cutaneous bruising, and this was not present.

The rapid return of voluntary power and of sensation on the third day after the injury, and the patient's ability to get out of bed and walk, when urged to do so, on the fifth day, in connection with the other manifestations of the case, make the diagnosis of the symptom-complex as one of hysteria positive.

I wish to express my indebtedness to Dr. Frazier for permission to report the case, and to Dr. Spiller for suggestions in the discussion.

BOOK REVIEWS.

Practical Dietetics, with Reference to Diet in Disease. By Alida Frances Pattee, Graduate, Boston Normal School of Household Arts; Instructor in Dietetics, Bellevue Training School for Nurses, Bellevue Hospital, New York City. Second edition, 1905. Revised and enlarged. Published by the author, 52 West Thirty-ninth Street, New York City.

This small volume should appeal especially to the graduate nurse, though it is not lacking in its application to the practising physician. After a short discussion on Food and Nourishment, about 170 pages are given up to the various methods of preparation of foods for the acutely sick and the convalescent; the remaining 80 pages treat of special diets in various diseased conditions.

On the whole the book is well written, the directions are clear and easily understood and it should be a valuable aid to anyone in charge of the preparations of food for the sick.

F. H. K.

A Text-book of Clinical Diagnosis by Laboratory Methods. By L. Napoleon Boston, A.M., M.D., Associate in Medicine and Director of the Clinical Laboratories, Medico-Chirurgical College, Philadelphia; formerly Bacteriologist of the Philadelphia Hospital, etc. Second edition, revised and enlarged, with 330 illustrations. Philadelphia, New York, and London: W. B. Saunders & Co.

A work which has reached its second edition in the short period of eight months does not need extended comment at our hands; this favorable reception is the best proof of its intrinsic worth and in time, no doubt, it will be found in the library of every practitioner. The revision, considering the short space of time having elapsed since the appearance of the first edition, has been thorough. Seventeen pages of new matter, covering the more important advances, have been added. These additions include descriptions of Biff's new hemogelometer, the Leishman-Donovan body, Ficker's method for diagnosing typhoid fever (this valuable method deserves a fuller description), Ravold's combined heat and contact test for the detection of albumin in the urine, Cammidge's reaction to differentiate the normal from the diseased pancreas (Opie's test, which is at least as valuable as Cammidge's, has been omitted), and a clear description of the method and clinical significance of cyto-diagnosis. We know of few works in which the individual subjects are given such full and clear descriptions as in this book. Doctor Boston is to be congratulated upon the success which has crowned this, his maiden effort.

E. L.

Examination of the Urine. A Manual for Students and Practitioners. By G. A. De Santos Saxe, M.D., Assistant Pathologist to the Columbus Hospital, New York; Member of the American Urological Association, etc. Fully illustrated. Philadelphia, New York, and London: W. B. Saunders.

This manual of 390 pages deals systematically and in detail with the whole subject of urinary examinations; at the same time an attempt is made to review briefly the physiology of urinary secretion, that the reader may be better able to interpret the results of his examinations. All extraneous matters and discussions of mooted questions have been wisely omitted and only methods which have stood the test of experience have been recorded.

Besides tests for the usual substances looked for in routine examination, a number of chapters are given to an elaboration of methods of examination for the more unusual substances in the urine. There are also several chapters on diagnosis of diseases of the kidneys and urinary passages, based on the urinary findings. At the end of each chapter is a series of questions emphasizing the important points. The type is clear and well spaced. The text is fully illustrated, including eight colored plates. The volume should be a valuable book of reference for the practitioner or the student.

F. H. K.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

THE FOCAL DIAGNOSIS OF OPERABLE TUMORS OF THE CEREBRUM.[1]

By Charles K. Mills, M.D.,

Professor of Neurology in the University of Pennsylvania; Neurologist to the Philadelphia General Hospital, and Consultant to the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases.

(From the Department of Neurology, University of Pennsylvania.)

INTRODUCTION.

In 1888, before the Congress of American Physicians and Surgeons, I presented a paper on cerebral localization in its practical relations, in which the status of focal brain surgery was discussed, the article including a consideration of the removal of brain tumors, and also of cortical excision and the operative treatment of hemorrhage, abscess and other lesions amenable to surgical procedure.[2] About this time and during a few succeeding years, the application of the principles of cerebral physiology to practical surgery attracted the attention and excited the enthusiasm of the profession in Europe and this country. Enthusiasm was dulled and attention relaxed by frequent failures in the attempts to exactly localize lesions, and by the difficulties which beset the surgeon in his efforts to remove these lesions with the trephine and rongeur.

Since the introduction of the osteoplastic operation and the newer researches into cerebral localization which have more clearly defined the motor and sensory regions of the cortex and the subdivisions of the association areas, the surgery of the brain has received a new impetus, the effects of which are seen in the increasing number of successful cases of operative interference reported in the last five or six years.

In a series of papers on localization and the neurology and surgery of brain tumors published during the last five or six years, I have given the results of many personal investigations.[3] This article is intended to summarize the more detailed studies of the papers referred to, presenting at the same time some new views and observations. It has been found necessary in several instances to change the positions and extensions of centres and areas as formerly given in accordance with newly obtained data. This is more particularly true with regard to the position and subdivisions of the motor area, a subject which has received full consideration at the hands of Dr. Frazier and the writer in a recent paper in the University of Pennsylvania Medical Bulletin.

[1] Read before the meeting of the Medical Society of the State of Pennsylvania, held at Scranton, Pa., September 26, 27 and 28, 1905.

[2] Transactions of the Congress of American Physicians and Surgeons, vol. i., 1888; also Brain, vol. xii., 1889.

[3] Tumor of the Superior Parietal Convolution, Accurately Localized and Removed by Operation. Journ. of Nerv. and Ment. Disease, May, 1900. (With Dr. W. W. Keen and Dr. Wm. G. Spiller.)

The Localization of Brain Tumors, Especially with Reference to the Parietal and Prefrontal Regions. Phila. Med. Journ., April 20, 1901.

The Separate Localization in the Cortex and Subcortex of the Cerebrum of the Representation of Movements and of Muscular and Cutaneous Sensibility. Journ. of Nerv. and Ment. Disease, November, 1901.

Tumor of the Brain Localized Clinically and by the Roentgen Rays, with Some Observations and Investigations Relating to the Use of the Roentgen Rays in the Diagnosis of Lesions of the Brain. Phila. Med. Journ., February 8, 1902. (With Dr. G. E. Pfahler.)

An Additional Case of Tumor of the Brain Localized Clinically and by the Roentgen Rays. Phila. Med. Journ., September 27, 1902. (With Dr. G. E. Pfahler, and Dr. J. B. Deaver.)

A New Scheme of the Zones and Centres of the Human Cerebrum, with Remarks on Cerebral Localization, Especially with Reference to Osteoplastic Operations for Brain Tumor. Journ. of the Amer. Med. Association, October 4, 1902.

The Surgery of Brain Tumors from the Point of View of the Neurologist, with Notes of a Recent Case. Phila. Med. Journ., November 29, 1902.

The Physiological Areas and Centres of the Cerebral Cortex of Man, with New Diagrammatic Schemes, University of Pennsylvania Medical Bulletin, May, 1904.

A Glance at the History of Cerebral Localization, with Some Considerations Regarding the Subdivisions of the Areas of Representation of Cutaneous and Muscular Sensibility and of Concrete Concepts. Proceedings of the Phila. Co. Med. Soc., September 30, 1904.

Subdivisions of the Concrete Concept Area of the Human Cerebrum. The Med. News, November 5, 1904.

The Diagnosis of Tumors of the Cerebellum and the Cerebello-Pontile Angle, Especially with Reference to their Surgical Removal. New York Med. Journ. and the Philadelphia Med. Journ., February 11 and February 18, 1905; also Philadelphia Hospital Reports, vol. vi., 1905.

The Motor Area of the Human Cerebrum; its Position and Subdivisions, with Some Discussion of the Surgery of the Motor Region. University of Pennsylvania Medical Bulletin, July–August, 1905. (With Dr. Chas. H. Frazier.)

GENERAL SYMPTOMS.

The general symptoms of brain tumor, which for completeness should receive brief preliminary consideration, are, as is well known, headache, vertigo, nausea or vomiting and optic neuritis. All of these may be present at one time or at some period during the progress of the case. In rare instances all of them may be absent, or one, two or any number of them may be present or absent. Their absence, severally or together, is therefore not conclusive against the existence of an intracranial growth.

The localization of headache cannot be depended upon as an indication of the site of a tumor. While the pain in the head caused by the presence of a brain tumor is often severe and may be agonizing, the complete or almost complete absence of headache is at times remarkable. This absence of headache is not always to be explained by the tumor being soft or deep-seated. In a recently observed case of tumor of large size and moderate firmness, the growth being adherent to the membranes, pain in the head was never suffered. Most frequently headache is absent in those cases of tumor which are subcortical and infiltrating, and of a consistency not much different from that of the brain itself. It follows that while the presence of severe pain in the head is strongly confirmative of the diagnosis of brain tumor, its absence cannot be regarded as excluding this diagnosis.

The same statement might be made with regard to optic neuritis, although it is more frequently absent than headache, at least this has been my own experience. It is probable that optic neuritis would almost always be found if the patient remained under observation until death, especially if operation was not performed. The reader is referred to Dr. G. E. de Schweinitz's paper on the "Ocular Symptoms of Tumor of the Cerebrum," published in this issue of the UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN, for a full discussion of this subject. Vertigo is rarely absent, but is often so little expressed or so little taken account of by the patient as to not attract the attention which it deserves. Nausea and vomiting, although often present and frequently presenting typical features, as for instance, their occurrence without accompanying signs of gastrointestinal irritation, are, on the whole, at least for long periods, as often absent as present.

When headache, optic neuritis, vertigo and nausea and vomiting are all present and persistent in the same case, the tumor is likely to be connected with the dura, and therefore accessible if situated anywhere on the brain convexity, the exceptions being cases of subcortical tumor of large size and great density.

A word might be said about the comparative importance of general and focal symptoms. The latter may, on the whole, be regarded as the more important of the two, although the presence of a general symptom, such as optic neuritis, may be the firmest link in the chain of evidence. Vertigo and nausea and vomiting are never absolutely conclusive, although they are not infrequently the symptoms which first suggest the existence of a tumor.

BRAIN TUMORS, PHYSIOLOGICAL AREAS AND SURGICAL OPENINGS.

Tumors and vascular lesions, such as hemorrhage, thrombosis, and embolism, tend to focus in special physiological areas. A tumor nearly always starts in what might be termed the heart of such an area, and largely occupies one such physiological region to the exclusion of others, although of course it may invade in any direction from its initial focus.

Following the old anatomical subdivisions of the brain into frontal, parietal, occipital and temporal lobes, these lobes can be conveniently subdivided for the purpose of diagnostic study and operative procedure into six areas, as follows: (1) the prefrontal or higher psychic; (2) the midfrontal or intermediate psychic-motor; (3) the postfrontal or motor; (4) the parietal or sensori-stereognostic; (5) the parieto-temporal or visuo-auditory; and (6) the occipital or visual. Each of these operable regions has its special symptom complex. It has also, from the surgical side, the special opening which will uncover it to best advantage.

With regard to the designation intermediate psychic-motor which has been applied by me to the second or midfrontal area, while this term is not altogether unobjectionable, it serves to express the idea that the functions of this region are intermediate between those of the purely motor zone and the region of higher psychic activity. Skilled movements of the upper and the lower extremity and of the musculature concerned with speech which are represented in this midfrontal zone, require constant guidance of purely motor stimuli by higher mental faculties as attention, comparison and reasoning, which are represented in the prefrontal lobe.

THE DIFFERENCE BETWEEN THE FUNCTIONS OF THE RIGHT AND LEFT CEREBRAL HEMISPHERES.

In the consideration of focal cerebral diagnosis some attention must be paid to the subject of the difference between the left and the right hemispheres. In the human race the left hemicerebrum, with rare exceptions, is the leading half of the brain, and as a rule the higher the indi-

vidual development, the greater will be the disparity between the two hemispheres in favor of the left. In children this difference is not so marked as in those of more mature years, and in the laboring classes not so decided as in those who pursue mechanical arts requiring special skill, while in the latter it is not so pronounced as in those of high intellectual capacity and acquirements. With regard to the last two classes, however, it must be remarked that in those who pursue mechanical arts or other vocations chiefly concerned with the concrete, the concrete memory field of the cerebrum may proportionately have a higher development than in those whose pursuits are esthetic, philosophical or ethical. In the latter the prefrontal or higher psychic region has its highest evolution.

It is scarcely necessary to do more than allude to the preponderant part played by the left hemisphere in the faculty of speech, and to call attention to the corollary that while lesions of this hemisphere, according to their location, may destroy respectively or conjointly the forms of sensory, conceptual or motor speech, those of the right hemisphere may leave these functions untouched or only transiently affected. The exceptions in the left-handed, or even in extremely rare cases in others, must of course be borne in mind.

In the case of speech and writing, the conclusions in the pages which follow are largely for the left hemisphere alone. Motor aphasia, motor agraphia, word blindness, word deafness, paraphasia, paragraphia, dyslexia, alexia, anomia and other disorders of speech and writing constituting parts of the focal syndromes which will be presently considered are to be referred entirely to disease of the left hemisphere. It is for this reason that tumors and other lesions of the right hemisphere are sometimes not so easy of focal diagnosis as those of the left. While destructive lesions of the left temporal lobe give symptoms readily traced to their anatomical seat, the right temporal lobe is one of the most latent regions of the brain.

The remarks here made, with regard to the difference between the functioning of the left and the right hemispheres, have their least application in a study of the local symptoms resulting from tumors situated in the primordial zones. Symptoms referable to the motor zone as now defined by the writer, namely, that region chiefly represented by the precentral gyre and the precentral portion of the paracentral lobule, have for the purposes of focal diagnosis almost equal value for either the right or the left side; in other words, a lesion of either the right or the left precentral gyre will give contralateral symptoms of definite type. In like manner a lesion of the primary or lower visual area, that is, of the calcarine fissure and cuneus of either side, will give almost identical contralateral symptoms. The same is true of lesions of the primary auditory olfactory and gustatory centres, remembering with regard to the primary auditory centre that word hearing is not a function of this centre, but of the higher auditory area contiguous to it, this being a part of the concrete concept area. The cortical representation of cutaneous sensibility and the muscular sense may be somewhat more highly evolved on the left than on the right side, but in the main it is true of the areas supplied with projection fibres that their cortical centres are equally developed in each hemisphere. Some facts seem to indicate that in the case of common sensibility one hemisphere has a larger power of representing both sides of the body than in the case of other functions.

Object recognition has a higher evolution in the left hemisphere than in the right, although both hemispheres take large part in this function. It follows that destruction of both occipital lobes or of parts connecting them is necessary for the production of complete and permanent mind blindness, and yet transient mind blindness may occur from a large lesion in the left occipital region.

Both prefrontal regions take part in higher psychic activities, but carefully collected data regarding lesions of the prefrontal lobes indicate that the left prefrontal region plays a more important role in intellection than the right.

I have closely studied the symptomatology of special cases of lesion of the left and the right parietal lobes, and in a previous paper have stated my belief that stereognostic conception probably has a higher evolution in the left hemisphere. A lesion of the posterior and superior portion of the right parietal lobe may therefore not give astereognosis of so decided a character as one in a corresponding position in the left parietal lobe, although the stereognostic function must have considerable development in both hemispheres.

From what has just been said about the difference between the functional power of the two hemicerebrums, this must be taken into most account when considering tumors or other lesions presumably present in the lower, intermediate and higher association areas of the cerebrum.

GENERAL REMARKS ON THE DIFFERENTIATION OF CORTICAL AND SUBCORTICAL TUMORS.

A brain tumor, like most massive lesions of the brain, is rarely strictly limited either to cortex or subcortex. If the neoplasm begins in the subcortex as a rule it spreads eventually to the surface; if, on the other hand, it originates in the dura or in the pia arachnoid it first compresses and then destroys the cortex and sooner or later destructively invades the subcortex. The clinical consequence of this joint involvement is that usually a sharp line of demarcation cannot be made between the symptoms of cortical and subcortical tumors at the time when the

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cases are under observation; nevertheless, a tumor springing from the membranes gives early and predominating cortical symptoms, while one arising in the centrum ovale gives early and predominating subcortical symptoms. The localizing symptoms of each subcortical region are correlated with those of the physiological cortical area to or from which the fibres of the subcortex come or go.

The question of the diagnosis of subcortical growths is one of great importance. Of course, speaking generally the term subcortical is applicable to all growths situated below the cortical cinerea, and in this sense might include not only tumors of the corona radiata and internal capsule, but also those of the basal ganglia, crura, pons and oblongata. These subcortical regions must, however, be separated, in order to come to any practical conclusions in differential diagnosis.

It is necessary therefore to distinguish two classes of coronal tumors—those which grow from within outward and those which invade from the cortex inward. The latter include entirely accessible tumors and will later be fully considered. As the subcortex is destructively invaded, the symptoms at first transient and recurring, such as agraphia, aphasia, paresis, astereognosis, word blindness or word deafness, become more and more persistent and permanent. As each separate cerebral area is discussed, some attention will be paid to the differentiation of tumors predominatingly cortical or subcortical.

It may be said that tumors, like other lesions of the corona radiata, will present variations in their symptomatology according to the relative number and particular value of projection, association, and commissural fibres in the part of the subcortex which is the seat of disease—a point to which some consideration will necessarily be given in the remarks on differentiation. Where projection fibres predominate, as in the subcortex of the motor and of the visual auditory and other regions of the special senses, the symptoms referable to irritation or destruction of these fibres will overshadow in importance in the study of the case those referable to implication of the fibres of association, and the focal diagnosis will chiefly depend upon the interpretation of the former. In the great association areas, posterior and anterior, the sensorial and motor symptoms will be more or less relegated to the background, although in the case of a tumor, this not infrequently involves some part of the projection system, as for instance the optic radiations, because of the manner in which they pass from the basal centres to their primary cortical destinations. Peculiar variations in symptomatology, no doubt, arise because of the disruption of the commissural connections between the two hemispheres, through the callosum and commissures; but the symptoms of such lesions rarely play an important part in practical focal diagnosis, although some exceptions to this statement need to be noted, as when considering such symptoms as cortical and subcortical word blindness, or such a question as that of object blindness being due to a lesion of one or both hemispheres or of the tracts uniting these hemispheres.

TUMORS OF THE PREFRONTAL LOBE, THE HIGHER PSYCHIC REGION.

Beginning at the anterior pole of the cerebrum, the first physiological region of diagnostic and surgical importance is one concerned with the highest functions of the brain. On the lateral aspect of the hemicerebrum it reaches from the anterior tip to a line drawn from a point about half an inch in front of the anterior branch of the Sylvian fissure (the pre-Sylvian fissure) nearly vertically to the mesal edge of the hemisphere. Its posterior boundary is therefore the midfrontal or intermediate psychic motor region, occupying the posterior portions of the first, second and third frontal gyres. Tumors if destructive, or other destructive lesions of the prefrontal lobe, and especially of the left prefrontal, will cause symptoms indicative of interference with the highest psychic functions. One of the chief difficulties in determining the exact functions of this region has resulted from inaccurate or imperfect observation of mental symptoms due to lesions situated in various portions of the brain.

It has occurred to me several times to examine patients suffering from brain tumor, in whose cases psychic symptoms have been noted, and in a few instances have been given localizing value, but without due consideration. The pain, distress, irritability, inattention, and mental confusion so commonly caused by a brain tumor wherever situated are set down as symptoms due to disturbance of the higher psychic functions, while in fact they are simply the expression of exhaustion and physical suffering, or of these together with impairment of concrete memories and powers of expression. The symptoms which are really referable to destructive lesions of the prefrontal portions of the cerebrum are best expressed by stating them to be evidences of higher psychic dissolution, which is shown in loss of memory and of powers of attention, abstract conception, comparison, judgment and higher imagination.

As in this contribution I am concerned almost exclusively with the focal diagnosis of brain tumor with the view of fixing the site of operation, I shall not go at any length into a discussion of disputed points in cerebral localization. Recently, in a paper with Dr. T. H. Weisenburg,[1] the question of the localization of the higher psychic functions with especial reference to the prefrontal lobe is discussed

[1] Chas. K. Mills and T. H. Weisenburg, Journal of the American Medical Association, vol. xlvi., Feb. 3, 1906.

with the report of a case of brain tumor with necropsy, the record of which favors the view of the existence of a higher prefrontal psychic area. This subject has also been discussed by me in other publications.

The morphological and anatomical observations show that the cephalic extremity of the cerebrum in the human being is concerned with functions of higher psychic valuation than that of any other cerebral region. Embryological investigations show the absence of projection cells and fibres in a region structurally rich in cellular association systems of an unusual order.

Many clinico-pathological investigations apparently contradictory to the view here expressed regarding the functions of the prefrontal lobe have been adduced, from the famous American crow-bar case to the most recent so-called digests of cases of brain lesion showing psychic symptoms. These can be passed by for the present with the assertion that they are not conclusive, which appears the more evident the more closely the compilations are examined. Cases confirmative of the view that the prefrontal region and especially the left prefrontal is concerned with the highest psychic functions have been collected in large number.

In order that any decided effect upon the mentality of the individual shall result, the lesion of the prefrontal lobe must be destructive and must be of some extent. A tumor growing from the dura may produce no psychic symptoms of importance except those which are the result of irritation or tension until it has destructively invaded the brain substance.

Such destructive invasion occurs as soon as occluded or obliterated vessels cause necrosis of brain tissue. The victim of such a destructive prefrontal lesion begins to show failure of memory which becomes more and more decided as the disease advances. This failure of memory relates more to matters abstract, general and distant than to those connected with his immediate surroundings. The power of attention, and especially of sustained attention, may be decidedly impaired from an early period. Problems formerly easy to solve become impossible. Inhibition is impaired. Hesitation, uncertainty, lack of force, slowness in apprehending and in communicating ideas, and motor disquietude due to loss of control, may be present.

Tumors of the orbital surface of the frontal lobe give especially psychic, olfactory and optic tract symptoms.

Some attention should be paid in this connection to the not infrequent occurrence of indirect and distant symptoms of a pronounced character. A frontal or prefrontal tumor may give severe occipital pain or the reverse may happen —a cerebellar growth causing frontal pain. Cerebellar or cerebellopontile symptoms have been noted in a few cases of prefrontal tumor, these being of large size and of such density as to exert considerable pressure. Collier,[1] for instance, has called attention to such a case of prefrontal tumor in which the only bulbar lesion present was degeneration of the eighth nerve. The patient's main symptoms after the disease had existed for seventeen months were paralysis of the left external rectus, marked nystagmus with a slow movement to the left, complete left nerve deafness, left peripheral facial paralysis, left cerebellar position of the head (head inclined to left shoulder and face rotated to the right), marked head retraction during paroxysms of pain, bilateral ataxia with lurching to the left, and diminished right knee-jerk. Necropsy revealed glioma of the right prefrontal lobe. The cerebellum especially the left lateral lobe was much indented into the edge of the foramen magnum.

While attention is called to the extraordinary symptomatology of this case, and while the possibility of the occurrence of a similar case with a like symptomatology should be borne in mind, too much stress should not be laid upon it in the study of focal diagnosis.

I have never seen a well-marked case of a so-called frontal ataxia, although it doubtless exists and may be due, as has been suggested, to involvement of the fronto-cerebellar tracts. Cases of agenesis and of lesions of the prefrontal lobe with some ataxia have been recorded. When present, it may be a symptom of inattention or of lack of judgment with regard to the movements rather than a true ataxia such as is seen in cerebellar or in postparietal disease. At a late period in the history of the case of prefrontal tumor which I reported with Dr. Weisenburg, the patient had a shuffling gait and was unable to convey food to his mouth with any certainty. Soon after he began to have muscular tremors in his hands and legs much like those seen in paralysis agitans.

On several occasions at periods separated by months, I saw in consultation a case which seemed to have some points in common with the one recorded by Collier, and which was eventually proved by operation and necropsy to be one of tumor of the right prefrontal and midfrontal region; it was situated so that its posterior limits grazed or merged into the motor region. The cerebellar and cranial nerve symptoms may have been due in part to counterpressure and traction.

The most important symptoms in this case were: (1) general enfeeblement; (2) what appeared to be bulbar and other cranial nerve symptoms, including dilated left pupil, sluggish iritic reflexes, left ptosis, and other third nerve palsies, nasal voice, some difficulty in swallowing, facial paresis on the left, drooling, and partial atrophy of the tongue; (3) ataxia with paresis of left upper extremity, paresis of right lower extremity, probable ataxia of left lower extremity, and

[1] James Collier, The False Localizing Signs of Intracranial Tumor, Brain, 1904, part iv.

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inability to walk or even stand without support; (4) marked Babinski reflex on the right and normal, although not over-prompt, plantar reflex on the left; and (5) impairment or loss of control over bladder and bowels. This patient on several occasions at long intervals had attacks of Jacksonian epilepsy, the spasm being usually most marked in the left side of the face and in the left upper extremity.

With regard to the prefrontal lobe, as this terminal zone contains no projection fibres, the symptomatology of tumors of the cortex and subcortex will not differ sufficiently to allow marked clinical distinctions to be made. Tumors of the membranes, as already indicated, simply compress the prefrontal lobe and may not exhibit a symptomatology of sufficient distinctness to allow them to be diagnosticated. The more and more the prefrontal subcortex is destructively invaded the more and more serious will be the symptoms of higher psychic dissolution.

TUMORS OF THE MIDFRONTAL OR INTERMEDIATE PSYCHIC-MOTOR REGION.

A tumor occasionally develops with its initial nidus in some part of what has been designated in our scheme as the midfrontal or intermediate psychic-motor region. The physiological centres and areas included in this region are the speech centre of the hinder part of the third frontal convolution, the graphic centre in the posterior part of the second frontal convolution, and the centres for movements of the head and eyes, intermediate between the speech and writing centres. A case of tumor involving this region was recorded by McConnell.[1] The symptom complex in such a case, if the left hemicerebrum be involved, usually has for its central phenomena motor aphasia, motor agraphia, and Jacksonian epilepsy, with movements of the head or of the head and eyes as a salient feature of the local spasm. The Jacksonian epilepsy includes spasm of the facial musculature and movements of the upper extremity. Some psychic symptoms of a special sort may be present, these being attributable to involvement of the prefrontal region. In McConnell's case, the patient's power of sustained attention and his memory were transiently affected. If the motor region is not directly involved, paralysis of the face and of the extremities is not present, or only to a slight extent. In McConnell's case some facial paralysis was detectable, but the arm, although decidedly affected in the spasmodic attacks, showed scarcely any impairment of motility. In this case the growth was successfully removed by Dr. Chas. H. Frazier, the patient recovering from his agraphia and his moderate facial articulatory paresis. His mental symptoms also cleared up entirely.

The difference of opinion and the disputes which have arisen regarding the existence of a separate motor graphic centre probably have their origin in part in misapprehensions of exactly what is meant by such a centre. Agraphia like aphasia may arise from lesions situated in different functional regions of the cerebrum. A cortical visual agraphia may, for instance, be due to a lesion of the centres for word seeing and letter seeing in the angulo-occipital cortex. An imperfect agraphia or paragraphia may be dependent upon destruction of tracts connecting the visual with the auditory centres, or connecting both of these centres with Broca's convolution. A form of agraphia results from a lesion of Broca's convolution. An aphasic who cannot arrange language for expression cannot write what he is unable to say, or can only do this very imperfectly. He may, however, be able to copy if sufficient time and care are taken. In one of my cases, the patient who had, as shown by necropsy, a lesion of the hinder part of the third frontal convolution and of the insula, could only write to a limited extent, but what he wrote was correctly spelled and expressed. If the posterior portion of the second frontal convolution is destroyed, the form of agraphia which results differs from that which is observed in the other instances just recited. The patient who may retain full powers of movement in his arm, forearm, hand and fingers, supposing his precentral convolution to be undestroyed, is not able to use these parts skilfully for the purpose of writing, and usually for other graphic purposes, as for drawing. The cerebral centre which controls the arrangement and coördination of these movements no longer exists, although the centre for the coarse movements, out of which they have been developed, may still be intact, as may also the centres for the arrangement and coördination of articulate speech.

In a case of midfrontal and postfrontal tumor seen by me in consultation with Drs. Weir Mitchell and John K. Mitchell, and operated on by Dr. Keen, agraphia was one of the most interesting symptoms. Other symptoms present were attacks of temporary aphasia, some evidences of psychic loss or change, twitchings, first of the right and then of the left side of the face, a few convulsive attacks and slight enfeeblement of the right arm. All the forms of visual and auditory aphasia, hemianopsia and disorders of sensibility were absent. Operation revealed a tumor which was of large size. The patient died of shock and hemorrhage, and a subsequent careful examination was made of the position and extensions of the tumor by Dr. William G. Spiller. The tumor was an endothelioma measuring 7 by 8 cm. The upper part of the precentral and the highest part of the first frontal convolutions were not com-

[1] J. W. McConnell, University of Pennsylvania Medical Bulletin, July-August, 1905.

pressed by the tumor. The lower posterior portion of the first frontal and the whole of the posterior portions of the second and third frontal convolutions and the lower two-thirds of the precentral except the extreme lowest part were all compressed beneath the growth. The tumor did not extend behind the central fissure and did not invade the brain tissue, but started apparently from the dura, pressing upon and causing thinning of the cortex and localized atrophy of the cerebrum.

In this case the agraphia present was peculiar and was briefly described by me in a letter to the doctors Mitchell, as follows: "The agraphia is certainly the most interesting clinical feature. In general terms it belongs under the head of motor agraphia, and a study of his writing gives some support to the view of those who have said that the so-called motor graphic centre might, perhaps, be better called an orthographic centre. He tends to repeat letters, syllables and words in writing, misspelling both common and proper names, evidently at times recognizing his errors and attempting by erasures and rewriting to correct them."

This case has been reported by Gordinier[1] from notes furnished by Dr. John K. Mitchell.

Tumors strictly limited to the hinder portion of the left third frontal convolution are rare, but such cases have been recorded. A tumor may originate in the preinsular portion of the Sylvian fossa, involving in its progress the third frontal and, perhaps, other contiguous regions. Such a case, while comparatively easy of diagnosis and accessible, may be difficult or impossible to remove. The effort should, however, be made and may be rewarded with success if the neoplasm should prove to be an enucleable dural growth. If the primary effects of the growth should be in the third frontal gyre the chances of success would be greater.

While tumors strictly limited to Broca's convolution are rare, this cerebral region is frequently involved by invasion. A growth beginning in the motor region may advance cephalad so as to involve both the second and third frontal gyres, or a prefrontal tumor may gradually encroach upon the posterior portions of the third, second and first frontal convolutions or either of these. The initial and the invasion symptoms must always be carefully studied in such cases.

Presuming the rare case of a tumor confined almost entirely to the third frontal gyre and preinsula, the symptoms will be those long described under the name of motor aphasia. The patient according to the destructive extent of the lesion will be unable to recall and arrange for use words, phrases and sentences. He may retain a few words or expressions, or have only a single recurring utterance; he may be able to write in proportion to the degree of his ability to arrange language for emission or projection. If the growth is strictly limited to the third frontal and insula he will not have agraphia of the form which is observed from destructive lesion of the graphic centre in the posterior portion of the second frontal. Even when the growth is somewhat closely confined to Broca's convolution some pressure symptoms may be present, and these will usually be in the form of paresis of the face or upper extremity. Jacksonian epilepsy of the aphasic-motor type may appear, and in this case the spasm will usually be ushered in by some repetitive speech disorder followed by facial or faciobrachial spasm, or even by hemispasm.

A few words might be said here about the effect of the involvement in a tumor or other lesion of the centres for movements of the eyes or of the head and eyes which lie between the graphic and motor speech areas, and to some extent in advance of them. Destruction of these centres interferes with the performance of skilled movements of all sorts. The part usually played by movements of the eyes and head in reading, speaking, writing, drawing, engraving, painting and similar pursuits will be disturbed. The guidance of skilled movements of the lower extremity such as are used in dancing, and of both the lower and upper extremities, as for instance those employed in fencing, will be impaired or lost.

The midfrontal region containing the centres for skilled and highly evolved movements of the upper extremity, of the head and eyes, and movements concerned with speech, probably is not furnished with projection fibres, although this question is not entirely settled. The centres for writing and speech probably have short neuronal associations on the one hand with the precentral motor centres, and on the other with the higher psychic centres of the prefrontal lobe; also of course they are associated with the sensory and concept centres of the cerebral zone of speech. The connections of these regions with the articulatory, phonatory and motor centres at the base of the brain and in the spinal cord are probably indirect through the centres of the motor zone.

The symptoms produced by midfrontal subcortical tumors can, it will be seen, scarcely be differentiated from cortical growths. Both will give clinical phenomena largely dependent upon the disruption of associations with other regions—psychic, motor and sensory. Aphasia, agraphia and disorders of the movements of the eyes and head will be present both in cortical and subcortical growths if these are of considerable dimensions. A tumor of the membranes invading the midfrontal cortex will however exhibit agraphic and aphasic symptoms of irregular and oscillating development, the patient retaining his powers of speech and writing later than in a case of destructive midfrontal subcortical tumor.

[1] H. C. Gordinier, American Journal of the Medical Sciences, September, 1903.

TUMORS OF THE POSTFRONTAL OR MOTOR REGION.

In the article by Dr. Frazier and the writer, already referred to, giving the results of faradization of the human cerebrum, the position is taken that the motor area is situated entirely cephalad of the central fissure, and is largely confined to the precentral convolution, its only extension beyond being an area for movements of the eyes and head in contiguous portions of the posterior extremities of the second and third frontal gyres. A large percentage of cerebral tumors originate in this region. It is scarcely necessary to discuss in much detail their focal diagnosis. The main symptoms are paresis, deepening into paralysis of the face, arm and leg, or of two or more of these portions of the body. The upper extremity is most frequently and most profoundly affected, movements of the leg, face, jaw and of the head and eyes being impaired in extent and degree in the order of the parts named.

At an early stage of the disease monospasm usually appears, and in most cases this has a distinct initial or signal symptom. A spasm may at first be confined to the part in which it begins, as to one side of the face, to the thumb, to the thumb and fingers, or to the thumb, fingers and wrist. Occasionally the initial symptom is in the lower extremity, showing itself, for instance, in a movement of the great toe or in an extensor or flexor movement of the foot. Almost invariably, as the tumor grows and the case develops, the spasm spreads. Facial spasm may for example have added to it spasm of all parts of the upper extremity; or convulsive movements beginning in this extremity may extend so as to involve either the leg, the face, or the eyes and head, or even all of these parts. The convulsion in the further progress of the case may become general, radiating to the other side.

Agraphia and aphasia on the one hand, or cutaneous and muscular paræsthesia and anæsthesia on the other, may be invasion symptoms.

Tumors strictly confined to the centrum ovale of the motor region are rare. A tumor beginning in the motor subcortex and up to the time of observation limited to it, will in the first place give symptoms of paresis or paralysis early, and these will be associated with tonic spasticity, Jacksonian spasms usually not being present. The tendency seems to be for spasms of the Jacksonian type to show themselves as soon as the motor cortex is invaded, either from within or from without, but this rule is not absolute, and a subcortical motor growth may give paroxysmal monospasm or hemispasm. When the tumor simply irritates the cortex, Jacksonian spasm may be present, although well-defined paralysis and tonic spasticity are absent; when the lesion is largely subcortical both paralysis and spasticity are marked clinical phenomena. A motor subcortical tumor is more likely than a cortical growth to have sensory symptoms associated with the disorders of motility, because the further the growth is removed from the surface of the brain the closer becomes the relations of motor and sensory tracts entering and emerging from the internal capsule. Reflexes in subcortical motor growths, as in cortical lesions, are exaggerated, but the ankle clonus and the Babinski response are if anything more persisting and striking phenomena in subcortical than in cortical lesions.

A tumor strictly confined to the motor region does not give objective sensory phenomena of a persisting character; the localizing symptoms of a growth so situated are motor, chiefly, as just described—paresis, paralysis and monospasm. Both the superficial and the deep reflexes on the side opposite to the lesion are abnormally exaggerated, much increased knee jerk, persistent ankle clonus and the Babinski reflex being commonly present. Hemianopsia, object blindness, speech disorders and true psychic symptoms are absent unless the tumor has greatly extended beyond the motor region.

In fixing the site of a tumor of the motor zone Jacksonian epilepsy plays an important diagnostic role, scarcely second in importance to monoplegia or hemiplegia. The significance of this form of spasm in focal diagnosis and the site and nature of the lesions causing it have been made by me the subject of another paper, to which the reader is referred.[1]

I shall summarize here a few of the most important points of this contribution. The term Jacksonian epilepsy is used in a broad sense as indicating monospasm or hemispasm due to cortical or subcortical discharge. It is by no means always due to gross lesion of the motor zone, although often an important sign of such lesion.

In hemiplegias due either to softening or hemorrhage, the cortex surrounding the gross lesion is often the seat of congestion and small extravasations, which irritating the brain substance and rendering it unstable, cause epileptiform attacks. These may take the form either of monospasm or of hemiepilepsy, and may be improperly regarded as caused by a tumor.

Many cases have been recorded in which Jacksonian epilepsy has been used in fixing the site of a tumor. Some of these cases reported by others or myself have been operated on successfully by Dr. Chas. H. Fraizer, Dr. W. W. Keen, Dr. W. J. Hearn, and other Philadelphia surgeons. In all of these cases, in addition to the Jacksonian spasm, other symptoms of tumor of the motor zone, such as monoplegia, exaggerated deep reflexes and the Babinski response were present; and if the cases were strictly localized to the motor area, sensory and psychic phenomena, and speech,

[1] Chas. K. Mills, The Significance of Jacksonian Epilepsy in Focal Diagnosis, with Some Discussion of the Site and Nature of the Lesions Causing this Form of Spasm The Boston Medical and Surgical Journal, April 26, 1906.

visual and auditory disturbances were absent. The general symptoms of brain tumor have usually been present, although I have seen cases of tumor of the motor zone in which headache and optic neuritis were not among the symptoms.

With regard to the seat and nature of the lesions and disturbances causing Jacksonian epilepsy, it must be borne in mind (1) that tumors situated in other parts of the brain than the motor cortex may cause Jacksonian epilepsy; (2) that other lesions beside tumors situated in the motor cortex may cause this form of spasm; (3) that it may occur in toxic and other diseases in which no demonstrable focal lesions are present; (4) that a spasm closely counterparting the Jacksonian type may be observed as a reflex or an hysterical disorder; and (5) that Jacksonian epilepsy may be simply an integral part or the entire expression of a case of idiopathic epilepsy. Each of these is fully considered in the paper to which reference has just been made.

TUMORS OF THE PARIETAL LOBE, REGION OF REPRESENTATION OF CUTANEOUS AND MUSCULAR SENSIBILITY AND OF STEREOGNOSTIC CONCEPTION.

In this connection the parietal lobe is defined after the usual manner of the anatomical works, namely, considered as regards the lateral aspect of the hemisphere, as that part of the cerebrum which is situated between the central fissure in front, the line of the parieto-occipital fissure behind and that of the Sylvian fissure below. It includes, therefore, the postcentral, superior parietal and inferior parietal gyres. This lobe can be divided physiologically into areas of representation of cutaneous and of muscular sensibility and of stereognostic conception, the first having its seat in the postcentral gyre; the second probably in the anterior portions of the superior and inferior parietal convolutions, and the third in the posterior portion of the superior parietal. Cutaneous and muscular sensibility and stereognostic conception probably all have some representation on the mesal aspect of the cerebrum, but we are only concerned with this indirectly in the present study of operable cerebral lesions.

The positive focal symptoms of parietal cortical and cortico-subcortical disease are impairment, usually moderate, of cutaneous sensibility, and especially of the pain and temperature senses, diminution or loss of muscular sensibility and astereognosis. When other symptoms are present they are commonly due to pressure or destructive invasion of environing regions with different functions. These may for example, if the tumor advances in a cephalic direction, be motor paresis and Jacksonian spasm with their usual accompaniments as regards the reflexes. Jacksonian spasm, however, as elsewhere indicated, occurs only rarely. If the growth invades posteriorly, the added symptoms may be visual aphasias, such as word blindness and letter blindness, and if inferiorly word deafness or other auditory aphasic phenomena. Any considerable implication of the cerebral subcortex posteriorly may give rise to hemianopsia.

If the tumor is strictly limited to the parietal lobe and does not cause any considerable pressure on the pyramidal system, both the cutaneous and the deep reflexes may be impaired in the direction of diminution. Not only is the Babinski response absent, but the cutaneous plantar response may be as negative as that which is observed in hysterical anesthesias. The knee-jerk and other tendon and muscle phenomena on the sides of the lesion remain normal, and on the opposite side either normal or somewhat depressed. If either by pressure or by destructive process, as the growth increases, the motor zone or the pyramidal tracts be involved, persistent ankle clonus and the Babinski response will appear. I have seen and recorded several cases in which the syndrome as regards the reflexes has changed during the progress of the case, as thus indicated.

To emphasize the most important features of the diagnostic symptomatology of tumors of the parietal lobe, it is necessary to briefly discuss the question of its subdivisions into different forms of sensorial and memorial representation. As I have long taught, the representation of cutaneous sensibility in all its forms is, generally speaking, located in such a manner as to surround the region of motor representation. As the motor zone according to our latest views is situated precentrally on the lateral aspect of the hemisphere, and also precentrally in the superior half of the paracentral lobule on its mesal aspect, cutaneous sensibility is in all probability represented in the postcentral convolution and in the lower half of the paracentral. As to how far the gyrus fornicatus takes part in this representation is not quite clear; not improbably the calloso-marginal fissure and the upper border of the gyrus fornicatus are concerned in cutaneous or muscular sensory representation, or in both. Cortical sensory representation is probably divided into segments for different cutaneous areas of the body, and these have topographical relations with centres and subareas of the motor region. The representation of cutaneous sensibility in the face, for example, is probably situated postcentrally and on a level with motor facial representation, that is, in the lower third of the postcentral and the adjoining anterior portion of the inferior parietal convolution, or the latter may be the seat of muscular representation for the face. The representation of cutaneous sensibility in the upper extremity occupies the postcentral convolution over a large area, extending from the facial representation to that of the trunk, this being subdivided for different parts of the upper limb. The representation of sensation of the trunk occupies a narrow strip like its correlated precentral motor centre, while sensation in the lower extremity, the anus and vagina is represented close

to the longitudinal fissure on the lateral aspect of the hemisphere and more largely in the posterior and inferior portions of the paracentral lobule and the adjoining limbic lobe. Just where, in the general sensory field, the different forms of cutaneous and of muscular sensibility have their separate cortical seats it is impossible, with our present knowledge, to say.

The views here expressed with regard to the subdivisions of the cortical sensory areas, to which should be added in this connection the area for stereognostic conception, have been held by the writer for some years. They were published in the *Proceedings of the Philadelphia County Medical Society* for 1904, and also presented in a paper before the American Neurological Association in the same year. Cases of cortical lesion have occasionally been published showing the restriction of disorders of sensation and of motion to one extremity or to limited portions of an extremity or the face, but the inferences drawn have usually been based on the view that the motor region was both postcentral and precentral.

In the well-known case of Starr and McCosh,[1] a limited postparietal lesion produced loss of muscular sense confined to the opposite arm and forearm without paralysis.

Spiller[2] has recently reported a case which indicates that sensation may be affected from a cerebral cortical lesion without motor paralysis, and that the sensory alteration may be confined to one limb. A few cases similar to those of Starr and McCosh and of Spiller have been recorded.

The writer holds in the first place that the cortical representation of cutaneous and muscular sensation is separate from that of movement; secondly, that it is distinct not only for face, arm, trunk, and leg, but also that special segments or areas of the skin are definitely correlated with subdivisions of the sensorial and stereognostic cortex; moreover, that the restricted centres and subareas for sensation and stereognosis are correlated anatomically and functionally with special cortical motor centres. In the periphery, segments of the skin are over or closely related topographically to the muscles producing movements which are represented in the motor cortex by centres which are connected with cortical sensory centres representing these cutaneous segments or areas. The segment of the skin covering the muscles producing adduction of the thumb, for instance, is represented in the cortex by a centre which is distinct but neuronally associated with the cortical centre for this movement of the thumb.

The parietal symptom complex as stated includes astereognosis, or as some prefer to call it, stereoagnosis, the recognition of the nature and use of objects by manipulation. This is not a sense like that of pain, contact, or temperature; neither is it entirely correct to speak of the function as stereognostic perception. Stereognosis is a conceptual process. The ability to recognize objects by touching and handling them so as to obtain an idea of their form is brought about by the recalling of memorial images obtained in the first place, through such senses as contact, pain, temperature, spacing, location and position, but although thus obtained the process of recognizing objects in this way becomes an independent one. The cutaneous and muscular sensory processes are primary; stereognosis is secondary and higher. The former are comparable to what takes place in the primary visual centres in the cuneus and calcarine cortex; the latter to the higher visual processes represented in the lateral occipitotemporal region. The stereognostic centre or area should therefore be situated in the concrete memory field or posterior association area of Flechsig. This is just where clinicopathological observation has placed it, namely, in the superior parietal convolution and the adjoining cortical expanse on the mesal plane of the hemisphere. This conceptual area, it will be seen, is surrounded on all sides by cutaneous, muscular and visual centres which administer to it. It is probable that in the process of stereognostic conception vision often plays a part; in other words in handling objects not only are cutaneo-muscular memorial images recalled, but also to some extent the visual concept of the object appears in consciousness.

A tumor rarely originates in and is still more rarely confined to the postcentral convolution. It is much more likely to have its primary nidus in the motor zone or in the postparietal region. It is for this among other reasons that ataxia and astereognosis are commonly more prominent manifestations in tumors of the parietal lobe than disorders of cutaneous sensibility. It is also likely that cutaneous sensibility has more or less bilateral representation in each hemisphere, so that destruction of both the right and the left postcentral gyres is necessary in order that decided cutaneous anesthesia shall be present.

With regard to tumors of the centrum ovale of the parietal lobe, of which I have seen several interesting examples, the differentiation between these and cortical neoplasms can be summarized in the statement that the disorders of cutaneous and muscular sensibility and of stereognostic conception are more persistent and complete in accordance with the depth of the destructive lesions, and with the additional statement that important invasion symptoms such as paralysis and tonic spasticity on the one hand, and hemianopsia and visual aphasias on the other, are much more likely to be present early in the subcortical growth.

In a case reported by Oppenheim[1] a man twenty-three years old had headache and vomiting with attacks of uncon-

[1] M. A. Starr and A. J. McCosh, Amer. Journ. of the Med. Sciences, Phila., 1894, vol. cviii.

[2] Wm. G. Spiller, Journ. of Nerv. and Ment. Disease, Feb., 1906, vol. xxxiii.

[1] Oppenheim, Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, 1900, 3d vol.

sciousness, after one of which he was left with paralysis of the left arm and left leg. The ophthalmoscope showed no optic neuritis. Pupils were normal and ocular movements were also normal. Examination showed that the ordinary use of the left arm was not much diminished, but hand pressure was slightly diminished. Tactile sense in the fingers and on the palmar surface of the hand was slightly diminished, as was also the sense of position. Disturbances of stereognostic conception were very pronounced in the left hand as tested with watch keys, steel pens and other objects. Sensations of pain and temperature were intact. In the left arm was a moderate but distinct ataxia. The left leg was dragged slightly in walking. The tendon reflexes on the left side in the leg were exaggerated to the extent even of a clonus. The left leg showed distinct ataxia. Hemianopsia was not present. Oppenheim's provisional diagnosis was tumor of the right parietal lobe reaching to the border line of the postcentral convolution and the first temporal convolution. The tumor was successfully removed. It was probably from description largely either cortical or corticosubcortical.

In 1905 Dr. Chas. H. Frazier operated on a case of gummatous meningitis with involvement of the cortex of the parietal lobe, a case which illustrates the principles of diagnosis for tumors or other irritative lesions of this region. The patient was under the care of Dr. Wm. G. Spiller, and had previously been operated on at the Philadelphia Polyclinic by Dr. John B. Roberts. For a time he was in the wards of the writer in the Philadelphia General Hospital. The case will be fully reported by Dr. T. H. Weisenburg at the meeting of the American Neurological Association in June, 1906. The main symptoms were diminution of cutaneous and loss of muscular sensibility, astereognosis and hemiparesis, and in addition the patient had frequently recurring attacks of Jacksonian epilepsy. The spasms began with a flexor movement of the fingers and adduction of the thumb, and then spread to the forearm, arm and shoulder, sometimes involving the face and abdominal muscles and very rarely the lower extremity. This case was interesting both as indicating the location of the areas for stereognostic conception, cutaneous and muscular sensibility and movements, and also because of the peculiar manner in which the impairment or loss of muscular sense and stereognostic conception was limited to portions of the hand.

In November, 1899, Dr. Keen operated for me on a case which illustrated the principles of diagnosis applicable in cases of tumor of the parietal lobe. The localizing symptoms were, in the main, impairment of cutaneous sensibility, loss of muscular sense, ataxia, astereognosis, paresis and ultimate paralysis. The patient had some verbal amnesia and fatigue on reading. At one examination he showed a temporary partial right hemianopsia. Reversals of the color fields and contraction of the fields for form similar to those supposed to be typical of hysteria were present at several of the examinations. The deep reflexes were exaggerated on the affected side and ankle clonus was present at a relatively early period after the recognition of the existence of a tumor. The Babinski response was not present at first; in fact, the metatarsophalangeal reflex was absent for a long time. Later the Babinski response appeared. Operation was performed with the view of uncovering the superior parietal convolution as the central point of procedure. The tumor was removed and the patient lived in comparative comfort for about five years, when there were signs of recurrence of the growth. Operation was again performed by Dr. Keen and a tumor at the site of the former lesion, but invading more anteriorly, was revealed and removed. The patient, however, succumbed to the shock of the operation.

In another case, a boy eight years old, operated upon by Dr. Keen, the chief symptoms were impairment of the muscular sense, ataxia, astereognosis and paresis. Cutaneous sensibility was unimpaired or but slightly affected, with the exception that he could not locate skin sensations accurately. The deep reflexes were all exaggerated on the affected side, ankle clonus and the Babinski reflex being present.

A tumor was found and removed by Dr. Keen, it being located in the main in the superior parietal convolution (parietal of Wilder).

In another case the patient early developed marked sensory symptoms. When examination was made, three weeks before operation, it was found that the pressure sense was absent all over the hand, that the pain and temperature senses were absent in the upper extremity, most markedly in some portions of it; that the Babinski reflex could not be obtained in the great toe, and the right arm-jerks were absent. Two weeks later the patient had a severe attack of tonic spasm in the right arm, which lasted fifteen minutes. Paralysis of the limbs of the right side, in a few days, was practically complete; no hemianopsia was present. The profound disturbances of sensation in this case were probably due to early implication of the parietal subcortex; the motor symptoms to subsequent invasion of the motor subcortex. Operation and necropsy showed that the tumor had invaded both subcortex and cortex of the parietal region and the subcortex of the postfrontal region; it had evidently originated in the subcortex, as it was just breaking through the parietal cortex at the time of operation. Operation in this case was performed by Dr. W. W. Keen.

In still another case recorded by me which was operated by Dr. W. J. Hearn, the first focal symptom was loss of power in the right leg. At the time of examination loss of power was marked in leg and arm, more complete in the latter, and some facial paresis was also present. Knee-jerk and patellar clonus were present on the right, although, strange to

say, both the ankle clonus and the Babinski reflex were absent. The right leg exhibited spasticity and tremor and the right arm was also spastic. Sensation to touch and pain was nearly lost in the right upper extremity; it was but slightly impaired in the right lower extremity. Impairment of muscular sense was also a marked feature. Astereognosis was present and became more and more positive as the case progressed to its termination. All forms of cutaneous sensibility and muscular sensibility were tested by the usual methods, with the result of showing impairment, which as time passed became more and more complete in the upper extremity. The so-called senses of locality, position, pressure and spacing were found wanting. In the right lower extremity the quadriceps-jerk and knee-jerk were exaggerated, and patellar clonus was marked. The focal symptoms became more and more profound, but did not alter except in degree. The patient suffered from headache of great severity and optic neuritis, which passed into atrophy. The diagnosis was made of a dense tumor of large size, probably in the main subcortical, situated chiefly in the parietal region, possibly invading the motor region and extending or compressing the posterior limb of the internal capsule and the optic radiations. The position of the growth was also determined by a Roentgen ray investigation, the shadow being very decided. In the operation performed by Dr. Hearn a portion of the tumor was removed.

Although this case eventually became cortical by its growth from within outward, it presented the characteristic features of a subcortical postfrontal and parietal growth—namely, early and marked paralysis, tonic spasticity without Jacksonian convulsions, loss of all forms of sensation and astereognosis; the reflexes, as might be expected, were of uncertain diagnostic importance because both the motor and the sensory subcortex were involved.

In a case of large parieto-occipital tumor the mistake of operating for the motor region was made. The patient was seen late, when the motor symptoms overshadowed all others, and one or two points in the past history of the patient were not obtained until after the operation, especially some facts which seemed to indicate that hemianopsia had been present. At the time when it was decided to operate, the patient's symptoms were such as to make it impossible to determine clearly the existence of symptoms like hemianopsia, astereognosis and impairment of cutaneous and muscular sensibility. Because of the predominance of motor symptoms, such as paralysis with contracture and exaggerated reflexes, it was decided to operate for the motor region, although the position of the growth was regarded as somewhat uncertain.

The general symptoms of brain tumor were present. The operation was performed by Dr. A. C. Wood, of Philadelphia. The patient died several weeks after the operation, and it was found at necropsy that the posterior line of the opening was just anterior to the large tumor mass.

TUMORS OF THE REGION OF THE JUNCTION OF THE PARIETAL, OCCIPITAL AND TEMPORAL LOBES, THE HIGHER VISUO-AUDITORY REGION.

The inferior parietal or subparietal convolution curves around the posterior extremity of the Sylvian fissure to unite with the first or supertemporal convolution, and in like manner another portion of the subparietal convolution curves around the posterior extremity of the first temporal fissure to join with the hinder portion of the second temporal convolution. Two angular or curving convolutions are thus formed. To that which is constituted by the convolution which winds around the posterior extremity of the first temporal fissure the term *pli courbe* or angular convolution has long been applied. The general region formed by the curving and uniting extremities of these parietal and temporal convolutions is one of the highest functional importance. It is the visuo-auditory area of the cerebral zone of speech. In the angular convolution, and perhaps extending somewhat beyond it posteriorly, are situated the centres for word seeing, letter seeing and number seeing. The primary auditory centre, that area the destruction of which on both sides will cause cerebral deafness to primary sounds, is situated in the retroinsular convolutions and the coterminus part of the posterior extremity of the first temporal convolution. The centres for word hearing and for other higher forms of auditory representation, as for natural musical notes and intonation, are situated on the outskirts of the primary region of auditory representation. The word hearing centre has been placed by me at the junction of the first and second temporal convolutions in their posterior parts. The centre for intonation is probably situated more anteriorly in the first or second temporal convolutions. With regard to the function of word hearing and of intonation, the representation is much more evolved in the left than in the right hemisphere.

A tumor destroying the angular or highest visual region will cause word blindness, letter blindness and number blindness, or some of these; also verbal amnesia, visual agraphia, paragraphia, alexia, dyslexia and paralexia. The chief invasion symptoms will be auditory aphasias and hemianopsia if the disease advances in a postero-inferior direction, or if in an antero-superior direction, astereognosis and disorders of cutaneous and muscular sensibility.

A tumor occasionally originates in the first or second temporal convolutions, of which I have seen instances. If such a growth originates in this portion of the left hemisphere the central feature of the syndrome will be word

deafness with its aphasic accompaniments, such as paraphasia, paralexia and word dumbness. Commonly some visual aphasia is associated with the auditory aphasia because of the proximity of the higher visual centres and their associations with the higher auditory centres.

Dr. Stanley Barnes[1] has reported an interesting case which illustrates the principles of focal diagnosis in a case of tumor situated so as to destroy or partly destroy the fibres which connect the visual and auditory centres together and these centres with the speech and graphic centres in the third and second frontal convolutions. A tumor was present which had evidently grown very slowly over a period of nine or ten years. The growth was bounded in front by the postcentral, and behind by the angular convolution, which was somewhat involved by young growth; above the superior parietal lobule was also somewhat implicated. It would seem from the description that the tumor occupied largely the inferior parietal convolution, although the recorder of the case speaks of it as bounded below by the supermarginal convolution. The patient had a series of attacks extending over many years. In these he was dazed or dizzy, had shimmerings of light before the eyes, and had numbness beginning in the right hand and extending to the arm, side and leg. Other symptoms were word dumbness, paraphasia, concentric contraction of the visual field on the side opposite to the lesion, and at times slowness in understanding what was said. Spontaneous writing, writing from dictation and from copy were all markedly affected. He had an imperfect right hemianopsia. He was not object blind, and had no loss of power or impairment of sensation or astereognosis. After the early seizures, the focal symptoms disappeared almost entirely, but were more persistent as time went on between the attacks. Optic neuritis was not present until late. Headache, vertigo and nausea and vomiting were among the general symptoms. The growth would probably have been largely included in the upper portion of the opening advised for the exposure of the visuo-auditory centre, and in the lower portion of the parietal opening. By moving the visuo-auditory opening a little forward and toward the mesal line the tumor would have been well uncovered.

MIDDLE AND INFERIOR TEMPORAL REGIONS.

Tumors are infrequent in the middle and inferior temporal regions, which include the lower half of the second and the whole of the third, fourth and fifth temporal convolutions. The uncinate and hippocampal convolutions are of course too centrally situated to be accessible to the surgeon. A growth involving the second, third and fourth temporal convolutions might be removed, at least in part, but in the case of the third and fourth temporal convolutions, not without some destruction of the brain substance around the tumor. I have seen a case of mid-temporal tumor which at an early stage, probably a year before the death of the patient, might have been removed by a careful surgical procedure. Such growths, like tumors in other situations, may arise in the membranes of the middle fossa and gradually compress and invade the temporal lobe. The symptoms produced by a tumor in the mid-temporal region are not well known. In one case studied by me they included word dumbness, hemianopsia and a partial mind blindness and word blindness. The tumor in this case, however, at the time of investigation just before death had invaded considerably toward the occipital lobe. A tumor strictly limited to the mid-temporal region will probably give as its main symptom word dumbness because of the destruction of the naming centre in this region, presuming its existence here. If such a centre should not here exist, as has been asserted, the same symptoms will be produced by destruction of the tracts passing through the various sensory centres on the receptive side of the brain to the motor speech centre in Broca's convolution.

The opening used in the effort to reach the middle and lower temporal regions should be made as low as possible on the side of the skull, its superior limit being on a line which would correspond with the horizontal branch of the Sylvian fissure just before it turns upward posteriorly.

TUMORS OF THE OCCIPITAL LOBE, THE LOWER AND HIGHER VISUAL AREAS.

The primary cortical visual centres, the centres of the optic perception field, are situated entirely or almost entirely on the mesal surface of the occipital lobe, the centres of color recognition being probably situated more ventrally on its tentorial aspect. The secondary or higher visual area, however, covers a large extent of the lateral occipito-temporal expanse. Centres of object recognition in its various forms are situated from the first to the fifth occipital convolutions inclusively and occupy also the contiguous caudal extremities of the adjoining temporal convolutions. These centres of object recognition, as has been indicated by me in other contributions, have probably a considerable subdivision, but the subareas or centres partly or wholly authenticated are few in number. They include the centres for word seeing, letter seeing and number seeing in the angulo-occipital region and centres for persons, places and natural objects in the rest of the lateral occipital lobe. I have suggested also the probable existence of centres for geometric and architectonic forms close to the representation of the

[1] Stanley Barnes, Review of Neurology and Psychiatry, vol. i. 1903.

symbols of language, but no facts have been forthcoming as yet substantiating this suggestion.

It is evident from a study of the anatomy of the skull and brain that only those occipital tumors are operable, or at least can be operated upon with much hope of success, which are situated wholly or largely in the lateral occipital region. It is true that the mesal surface of the lobe and even its tentorial surface may be to some extent explored, and by a good chance a small tumor may be shelled out of either of these regions. Another point worthy of recollection in this connection is that a large part of the occipital lobe may be removed, as was done in one of my cases by Dr. Frazier, without fatal or even serious symptoms, except of course the necessary loss of vision; so that a tumor situated in any part of the occipital lobe may be worthy of the consideration of the surgeon.

A tumor of the lateral occipital or occipito-temporal region, the area of higher visual representation, if the lesion be a left-sided one, will give for its main symptoms word, letter and number blindness, complete or partial, and if partial their accompanying aphasic defects such as paralexia, agraphia and paragraphia, optic aphasia or word dumbness, and in some cases mind blindness, which in unilateral lesions is usually incomplete and transient or paroxysmal. As tumors, even those which originate in the membranes, usually sooner or later involve the subcortex, hemianopsia is often present. Other compression and invasion symptoms are chiefly auditory symptoms, such as word deafness and paraphasia, although ataxia and astereognosis may appear if the growth advances forward. In addition to the hemianopsia, if its advance is subcortical, hemianesthesia and hemiparesis or paralysis may appear.

The Wernicke reaction is absent. The deep and superficial reflexes in the extremities are usually not changed. Motor affections and psychic disturbances except those concerned with visual concrete memories are absent.

In the last section I have spoken of the manner in which the highest visual and the highest auditory areas could be exposed jointly or separately. If the symptoms are almost purely visual the osteoplastic opening should be more posterior than those referred to in that section; in other words, it should be made so as to include the entire lateral aspect of the occipital lobe with adjoining extremities of the parietal and upper temporal convolutions, as indicated by the space marked occipital in Fig. 2. Practically the region referred to in this figure would be exposed by an opening one side of which would be parallel with the longitudinal fissure, about one-half inch from the mesal line, and the other parallel with the lateral sinus about one-half inch from the cranial line corresponding to this sinus. The other two sides of the opening could be made in the most convenient manner possible.

I have seen no cases of successful operation on the occipital lobe, although in two cases of occipital tumor operation was performed for me by Dr. Frazier. The growths, however, were not reached, probably because they were located tentorially or meso-tentorially. In one case the patient died, but no necropsy was allowed; the other patient is still living and in fair general health, although a portion of his occipital lobe was cut away several years since. This case is one of those referred to by Drs. Spiller and Frazier in their paper on "Decompression."

A tumor of the right basal occipito-temporal region, if the optic radiations and cuneus are not involved, is very difficult of diagnosis. In a case of this kind occurring in my practice, Dr. Frazier performed a subtentorial operation. This patient had the well-marked general symptoms of brain tumor, including optic neuritis of an extremely high grade. Hemianopsia, as tested by the hand, which was the only method which could be adopted owing to his relative blindness, was not present. The only symptoms which seemed to have any localizing value were a drooping of both eyelids and nystagmus on lateral movements. Associated upward movements were performed promptly, but the patient was unable to keep the balls upward, and convergence was very slightly performed. The tumor in this case was large and dense, and had destroyed the occipito-temporal region in large part.

GENERAL REMARKS ON SOME OF THE SOURCES OF ERROR IN THE FOCAL DIAGNOSIS OF BRAIN TUMOR.

In spite of the numerous advances, some of them quite recently made, in our knowledge of focal physiology and focal diagnosis, mistakes are still made by those whose business it is to locate tumors or other operable lesions for the surgeon, although it is notable that these mistakes are growing fewer. At several points in the preceding pages some of the sources of error in focal diagnosis of brain tumors have been pointed out, as, when speaking of the occurrence of cerebellar, sixth nerve and other symptoms because of the tilting of the brain, and its jamming into the foramen magnum by a prefrontal growth, as recorded in one of the cases of Collier; as also when referring to the fact that Jacksonian epilepsy may be simply a part of the convulsive attack in a case of idiopathic epilepsy, and that this form of spasm, due to a variety of focal lesions and general states, may be attributed to the presence of a neoplasm in the motor region; and again, as when speaking with references to illustrative cases, of the masking of parietal or prefrontal symptoms by the late and more obtrusive motor manifestations due to pressure and invasion.

The paper of Collier on the false localizing signs of intracranial tumor, to which reference has already been made

several times, presents in an admirable way the manner in which focal symptoms in cases of brain tumor may mislead the neurologist and surgeon. Almost every point to which he calls attention has been personally observed by me, and to some of the points I have called attention incidentally in various papers. The contribution of Collier has, however, particular value because of the succinct and eminently practical manner in which he has marshalled these false portents, and in the remarks which follow I shall again avail myself of his observations.

The interpretation of symptoms due to pressure exerted upon a functional area or tract as the evidences of tumor impairing or destroying this area or tract and the obscuring of the early and more important symptoms by those which are caused by late invasion or encroachment are matters upon which emphasis has already been made, but because of their importance it will be of service to refer to them again in this general discussion of diagnostic errors, especially as the neurologist is sometimes called late in the course of a case of brain tumor to decide as to the site and operability of the lesion. He may see the patient for the first time after the disease has been present, recognized or unrecognized, for months or even years. The patient at this time may present a striking symptom-complex. It may be that of hemiparesis or hemiplegia, with occasional attacks of Jacksonian epilepsy; it may be hemianopsia with some attendant sensory phenomena; or it may be aphasia or agraphia; or other symptoms formerly present may be overshadowed or obscured, as for instance, in a case of hemiplegia such clinical phenomena as hypæsthesia, ataxia and astereognosis, or in a similar case, psychical, aphasic and agraphic phenomena. It follows, therefore, that when the localization of a growth is for the purpose of exactly fixing the limits of an operation, the method in which the tumor has spread, as determined by a careful study of the history of the development of symptoms in the case, is often of the greatest importance. Probably the mistake most frequently made is that of supposing a tumor originating and largely occupying the prefrontal lobe, and only encroaching upon the graphic, speech or motor region, chiefly occupies the last.

Compression symptoms usually precede for a short time at least those of absolute encroachment, and this fact needs to be borne in mind. It may be said, however, that symptoms due solely to pressure are rarely absolutely continuous and can be differentiated by a close study of the case. In many cases the pressure seems to transiently let up or recede, probably because, in some cases at least, of the filling and emptying of the cysts which are often connected with tumors.

Collier's discussion of the disappearance of true localizing signs in late stages of brain tumor is in part a discussion of the effects of invasion. Among other things, he shows how the late symptoms may obscure entirely the presence of a cerebellar growth.

One must be always on his guard not to be misled in his efforts at accurate localization because of the presence of abducens palsy. Different theories in explanation of the frequent occurrence of this symptom have been given. Probably it has most often been attributed to the effects of pressure upon the nerve in its long intracranial course, and this doubtless accounts for it in some instances. Collier has suggested another explanation which is reasonable and may explain the symptom in some cases. He has shown that as the result of pressure of a large prefrontal tumor, the brain may be more or less tilted so that the cerebellum and oblongata are jammed into the foramen magnum. One of the consequences of this compression and tilting of the entire brain is traction on nerves like the sixth and third, which have a long caudocephalic course. The sixth nerve especially would be subject to such traction; in other words, the case would afford an illustration of indirect traumatic traction palsy. The nerves like the fifth, seventh, eighth and others which run transversely or more obliquely are not subjected to the same amount of traction. Whatever may be the correct explanation, the diagnostician should always bear in mind that while paresis or paralysis of the sixth nerve may be of strict localizing value, that is, may indicate involvement of this nerve, it may on the other hand be an indirect symptom of tumor of large size situated in various regions of the brain.

Fifth nerve symptoms, either sensory or motor, may be present in a case of brain tumor in which this nerve is not directly involved. In two cases referred to by Collier, in which the tumor was situated in the left prefrontal region and frontal centrum ovale respectively, fifth nerve anesthesia and hemianopsia were both present. Collier attributes the symptoms referable to this nerve to pressure exerted on the middle fossa by a large prefrontal tumor on the same side.

The occurrence of bilateral spastic paresis in a case of brain tumor is not infrequent and may be misleading. In one of my cases of tumor of the cerebello-ponto-oblongatal recess this symptom was most marked, and hydrocephalus of considerable degree was found on necropsy. So marked was the spastic paralysis in this case that I suspected some form of spinal disease, as meningomyelitis, in addition to the brain tumor which was evidently present from the general, as well as the local, symptoms. Collier lays much stress on the occurrence of this symptom of bilateral spastic paresis due to hydrocephalus accompanying a brain tumor in various intracranial situations. A tumor of the brain stem is most likely to give rise to this affection. Affections of various cranial nerves may be associated with the bilateral spastic paresis.

In discussing errors in focal diagnosis, the question of multiple tumors needs brief consideration. When more than

B.J.O.D.

Fig. 1.—Diagram showing the convolutions uncovered by standard osteoplastic openings for the prefrontal, postfrontal (motor), and parietotemporal (visuoauditory) regions.

Fig. 2.—Diagram showing the convolutions uncovered by standard osteoplastic openings for the midfrontal, parietal, and occipital regions.

one growth is present in the cranium, it is rare to find these growths in the cerebrum proper. Usually one will be present somewhere in the cerebrum, and another or others at the base or in the cerebellum. In multiple sarcomatosis, growths may, for instance, be present in both cerebellopontile recesses, in the middle and anterior fossa and even in various positions in the spinal canal. In very rare cases similar tumors may be present at nearly corresponding points in both hemispheres. A tumor of the callosum occasionally invades in both directions. In bilateral tumors, if recognized, operation on both sides might be considered; in other cases the growths are inaccessible and inoperable.

Our concern is with the operable tumors of the cerebrum, but a few words might be said about the diagnosis of some of those intracranial neoplasms which are inaccessible and inoperable, especially as in a few instances these give symptoms which may seem at some stage to point to accessible regions. Tumors of the thalamus give inco-ordination and anæsthesia, and according to some authorities central pain. If the pulvinar or optic radiations are involved hemianopsia will be present. When the superior cerebellar peduncles are included in the lesion hemichorea and hemiathetosis may be present, and when the pregeniculum is implicated the Wernicke pupillary reaction. Forced laughing or crying have also been noted as thalamic symptoms. Monoplegias or hemiplegias described in connection with thalamic lesions are probably due to the destruction of the neighboring parts of the internal capsule. A tumor involving the thalamus and posterior part of the posterior limb of the internal capsule might at some stage of its development have some of the appearances of a tumor of the parietal subcortex.

Tumors of the lenticula and caudatum give symptoms which cannot with our present knowledge be well separated from growths affecting the internal capsule. These symptoms are mainly hemiparesis or hemiplegia with disorders of speech, and if the lesion is in the caudal portion of the lenticula, hemianæsthesia may be present. Von Bechterew[1] has described a symptom of lesion of the lenticula designated by him as pseudoonclia paræsthetica. To a patient suffering from this affection the limbs appear to be in a position in which they are not.

With regard to tumors of the chiasm and the pituitary body, attention should be concentrated upon bitemporal hemianopsia, olfactory disorders and symptoms indicative of implication of the third, fourth and sixth nerves. The part which some believe is played by the lesions of the pituitary body in the causation of acromegaly should be borne in mind. In tumors of the crura, symptoms of third nerve involvement on one or both sides and paresis of the extremities on one or both sides are prominent. Chiasmic, pituitary or crural lesions can scarcely be mistaken for any form of operable lesion of the cerebral cortex or subcortex.

Tumors involving the cinerea of the region of the Sylvian aqueduct, the brain stem or the cranial nerves at the base anywhere in their course give pseudobulbar, nuclear and cranial nerve symptoms—a statement sufficient to indicate the method of their separation from operable cerebral lesions.

The symptoms of tumors of the pons will vary according to the exact location and extensions of the growth. Among them the most notable are alternating hemiplegias of different type, paresis or paralysis of separate or of associated ocular movements, dysphagia, anæsthesia, which may be of the crossed type, astereognosis in rare instances, painful affections of the trigeminus and vasomotor and thermic changes.

The chief symptoms of tumors of the quadrigeminum are impaired sight or hearing or both, paralysis of ocular movements, bilateral or associated, and inco-ordination especially in attempts to walk or stand. Other symptoms have also been recorded, such as nystagmus, automatic repetition of words, and a tendency to move backward or other forced movements. Focal symptoms referable to neighboring parts, such as the cerebellum and the ascending and descending tracts in the pons oblongata may be present and the general symptoms of a neoplasm, such as headache, optic neuritis, vertigo, nausea and vomiting, are usually marked.

As tumors of the cerebellum and the cerebellopontile angle have been discussed elsewhere by the writer and by his colleagues in the preparation of the present series of papers, attention will be directed to cerebellar growths only in the briefest possible manner. It should be remembered that an accessible parietal tumor may give ataxia as one of its prominent manifestations, but that a growth giving this symptom is to be differentiated from a cerebellar growth, causing ataxia by the fact that the ataxia is more likely to be confined to the extremities of one side, and especially to one upper extremity in parietal lobe cases, and that in the same cases, astereognosis and impairment or loss of cutaneous and muscular sensibility are usually present, these being absent in a cerebellar neoplasm. I would refer elsewhere, however, for a full consideration of this subject.[1]

With regard to the focal diagnosis of brain tumors from such lesions as abscess, hemorrhage and acute softening, from embolism or thrombosis, little need be said. The principles of diagnosis are the same as in the case of tumors. The differences in symptomatology depend chiefly upon the differences in the nature of the lesions, although in the case of hemorrhage and acute softening, the rapidity of develop-

[1] Von Bechterew, Neurol. Centralbl., No. 17, September 1, 1905.

[1] Tumors of the Cerebellum, New York Medical Journal and the Philadelphia Medical Journal, February 11 and February 18, 1905; reprinted with papers by Drs. Frazier, Weisenburg, de Schweinitz and Ludholz as a monograph.

ment is of some assistance in differentiation. An abscess may cause either more or less pressure than a tumor; probably when entirely confined within the brain substance, less rather than more. An abscess may be extracerebral that is, of the membranes, as for instance when in the middle fossa. In such cases the symptoms will not only be indicative of the physiological area disturbed or injured, but also of dural irritation, and it may be of disturbance of the functions of cranial nerves. The fact that an intracerebral abscess is often latent for a considerable or even a long time needs to be borne in mind. After all the differentiation between abscess and tumor will depend largely upon the history of probable causation, and upon the presence or absence of the indications of sepsis. In the presence of purulent otitis or of some other source of pus, abscess becomes more probable, and yet the diagnosis of abscess must not be reached simply in this way, as I have known not a few instances in which brain tumor was present in cases with the evidences of recent or old aural disease.

With regard to the diagnosis of hemorrhage from tumor the usually sudden occurrence of hemorrhage is an important point; it may also develop more or less slowly. It must be kept in mind that a hemorrhage sometimes takes place during the growth of a tumor, either into its substance or on its borders. I have seen instances of such hemorrhages in cases of gliomata and even of gummata. A point of value in the differentiation of hemorrhage from tumor is that in some cases of brain tumor, although the neoplasm has been long existent, the onset of focal symptoms of diagnostic importance is rapid. This is probably to be accounted for by the brain ceasing after a time to accommodate itself to the new-growth, and also by the sudden or rapid increase of its destructive influence on vascular regions invaded by it. Acute softening from embolism is always sudden, and embolic apoplectiform symptoms are of a special type. The presence of endocardial and valvular lesions or of other pathological sources of emboli will of course have great weight in diagnosis. In softening from thrombosis, which may be sudden or rapid in onset, although the changes in the vessels leading up to the attack may have been long present and increasing, the absence of the general symptoms of brain tumor and of the pressure and irritation symptoms are important.

The diagnosis, focal and general, of brain tumor from general paresis is sometimes difficult; it is especially so in cases of prefrontal tumor. In several instances I have hesitated and postponed operation because of this difficulty. In certain cases of general paresis, as is well known, the symptoms are of a quiet or apathetic type. The patient does not exhibit the extravagant optimism of the typical paretic. In a few cases most of the decisive spinal and cranial physical symptoms, such as changed knee-jerks, ataxia, and disturbances in the iritic reflexes, may be absent. The scene is dominated by dementia showing itself in loss of memory, disorientation, impaired judgment and lack of self-control. The speech disorders are never entirely absent, but unfortunately in the case of a prefrontal and midfrontal growth these may be present. In such a case the general symptoms of brain tumor if present are of the greatest value, but one or even all of them may be absent and yet a neoplasm be present. It is sometimes necessary to wait in such cases for the development of aphasia and agraphia if the tumor is left sided, or for Jacksonian epilepsy and paretic symptoms if right sided.

THE OCULAR SYMPTOMS OF TUMOR OF THE CEREBRUM.

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The ocular signs of tumor of the cerebrum are chiefly concerned with changes in the fundus oculi, particularly the nerve-head, and in less important degree with anomalies of the visual field, the pupillary reflexes, the external ocular muscles and the movements of the eyeballs. The present paper is concerned only with papillitis or choked disk, and a brief reference to the visual field phenomena.

PAPILLITIS OR CHOKED DISK.

(*a*) Frequency. It is a well-established fact that papillitis or choked disk is, headache excepted, the most common general symptom of tumor of the brain. It is, however, not possible to obtain accurate statistics as to its frequency, because, as has been well pointed out by Bruns and other observers, the available material represents examinations of the eye-ground at different stages. Therefore, absence of intraocular optic neuritis at one examination does not exclude its presence at a subsequent one.

According to John E. Weeks,[1] an average of the frequency of optic neuritis in brain tumor, as recorded by Oppenheim, Gowers, C. P. Knapp, Dana, Bernhardt, Martin and Bramwell, is 78.2 per cent., although higher percentages are found

[1] Transactions of the Section of Ophthalmology, American Medical Association, 1899, p. 322.

in individual series, for example: Oppenheim 82 per cent., Annuske and Reich 95 per cent., Kamplerstein 80 per cent. In my own experience, this symptom has been present in fully 85 per cent. of the cases examined.

Bearing upon this question and upon the relative frequency of papillitis in growths in various parts of the cerebrum, the analysis of the reports of 601 brain tumors by J. M. Martin[1] is important. He found that of the neoplasms in which optic neuritis was present at some time in the course of the disease, those which involved the corpora quadrigemina and the crura gave the highest percentage, namely, 100; next came tumors of the cerebellum and parieto-occipital region, with a percentage of 89; new-growths of the frontal region and those denominated "general" furnished a percentage of 84; following these were tumors of the basal ganglia, with a percentage of 75, of the pons and medulla and of the temporosphenoidal lobes, and "multiple," with a percentage of 68, of the centrum ovale, with a percentage of 67, of the pituitary body, with a percentage of 65, of the motor area, with a percentage of 62, and of the corpus callosum, with a percentage of 46. In his tabular statement of the growths in which optic neuritis was present excluding atrophic cases, those which involved the cerebellum gave the highest percentage, namely, 81; next the corpora quadrigemina, with 79 per cent.; the symptom was least frequently present in tumors of the pons and medulla and of the corpus callosum, viz., 36 and 25 per cent. respectively.

According to Oppenheim,[2] choked disk is relatively often wanting in tumors which proceed from the meninges and compress the brain, and in cortical tumors that do not sink deep into the white matter, while in growths of the pons, of the medulla and of the corpus callosum papillitis fails with tolerable frequency, or is late in its development. In so far as the failure of choked disk to appear in tumors of the pons and medulla is concerned, Bruns[3] is in accord with these statements, but he declares that it is apt to be lacking in tumors of the crura and of the corpora quadrigemina, in this respect differing utterly from Martin's statistics. J. M. Martin also draws attention to the comparatively small proportion of cases in which optic neuritis is found in tumors of the corpus callosum and of the pons and medulla, it being absent in nearly two-thirds of the cases.

According to the well-known analysis of Edmunds and Lawford[4] there is a comparative immunity from optic neuritis of the cases of tumor in the cortical motor area. Thus, they added all their cases (107 in number) in which the locality of the tumor was toward the convexity of the brain, that is, for example, in the anterior frontal convolutions, the motor convolutions, the occipital lobes, the hemispheres and the meninges at the motor convolutions, and found that they yielded 50 per cent. of optic neuritis, while those toward the base, that is, in the ganglia at the base, in the temporosphenoidal lobes, in the cerebellum, in the medulla and pons, and in the meninges not at the motor convolutions, yielded a percentage of 74 of optic neuritis.

The most recent contribution to this subject is by Kamplerstein,[1] who has collected 76 cases of brain tumor with choked disk in which an autopsy was made. The situation of the tumor was as follows: Frontal lobe twelve times, temporal lobe six times, parietal convolution four times, occipital lobe five times, epiphysis twice, third ventricle twice, corpus callosum three times, optic thalamus twice, corpora quadrigemina seven times, hypophysis three times, fourth ventricle once, peduncle of the cerebellum twice, cerebellum twenty-three times.

(*b*) Date of Occurrence and Character of the Neuritis and Nerve-head Changes. As may have been inferred from the previous paragraphs, and as is apparent from the investigations of Oppenheim, Bruns and others, optic neuritis or papillitis, if it does not fail entirely as a symptom of tumor of the pons, of the medulla and of the corpus callosum, is late in its development and this lateness of development is also to a certain extent, true of tumors of the frontal lobe and the parietal convolutions. Indeed, papillitis of brain tumor, and by this is meant of the cerebrum and not of the cerebellum (for the latter portion of the intracranial contents is not now under discussion), is not an early symptom if the visual tracts at the base of the brain are excepted.[2]

It is not possible to predict how soon after a tumor arises optic nerve changes will appear. Sometimes the whole process from the beginning of papillitis to the height of its swelling is complete in a few weeks, sometimes several months may elapse. (Bruns.) I have known optic neuritis to be postponed until within a week of the patient's death, although all the symptoms of brain tumor had been present for more than a year. In general terms, however, it may be stated that, with the exceptions already noted, the process must have existed for some time and the increased intracranial tension have lasted for a definite period before either an engorgement œdema of the optic disk or an inflammatory optic neuritis develops.

In a certain number of cases it is possible to watch the development of neuritis from its very earliest stages. The first

[1] The Lancet, ii. 1897, p. 83.
[2] Die Geschwülste des Gehirns, Wien, 1896.
[3] Die Geschwülste des Nervensystems, Berlin, 1897.
[4] Trans. Ophth. Soc. of the United Kingdom, iv. 172.

[1] Klin. Monatsbl. f. Augenheilk., Bd. i., 43, 1905.
[2] It must not be forgotten that the optic neuritis of cerebellar tumor is often an early symptom and develops with great rapidity. The Ocular Symptoms of Cerebellar Tumor, by G. E. de Schweinitz, New York Medical Journal and Philadelphia Medical Journal, Feb. 11 and 18, 1905.

symptom is increased redness of the disk and obscuration, usually of its upper and lower borders, associated with a certain turgescence and inequality of the venous circulation. Occasionally the nasal border is earlier and more obscured than the other margins in the form of the so-called hemineuritis. Usually within a week, the obscuration of the nerve edges increases and the temporal border becomes veiled, while a distinct swelling of the nerve-head appears and the darkness and tortuosity of the veins is decidedly more manifest. At this period the difference in level between the top of the swelling papilla and the eye-ground is usually not more than 1.5 or 2 D. Within the next week there is complete loss of the light spot and complete obscuration of the disk, the swelling increases, assumes a mound shape of mixed grayish-red color, and finally the form of the disk is entirely lost and its position can be inferred only by the convergence of the vessels. Not infrequently at this stage, and indeed at an earlier one, linear hemorrhages appear in the immediate neighborhood of the disk or on its swollen surface. The arteries, smaller than normal, pursue a moderately straight course and are difficult of recognition, being partly concealed by the swelling. The veins are dark in color, distended and tortuous, and pass along the slope of the elevation, often dipping into the infiltrated tissue.

The height of the papillitis varies, usually between 3 and 6 diopters. Occasionally it is as high as 8 or 9 diopters, and in a recent case, seen in consultation with Dr. Weisenburg, the swelling of the disk was 11 diopters. Indeed, some of the prominent vessels were still in focus when viewed through a 12 diopter convex lens. This is the highest elevation that I have seen in the choked disk of brain tumor. The exact position of this tumor was not located. It was probably in the cerebellum.

At some periods of optic neuritis, especially in the later stages, there may be very great increase in the number of hemorrhages, both on and in the immediate neighborhood of the disk. Exudates may also appear, white or yellowish-white in color, and white patches develop in and on the swollen disk.

To distinguish a true beginning neuritis or a congestion with œdema from a "spurious optic neuritis," or so-called "hyperopic disk," as it occurs in association with refractive error is often most difficult. There is, however, in the beginning of optic neuritis of brain tumor a certain quality which pseudoneuritis does not possess. The blurring of the disk edges is more complete, and even with the indirect method of examination the obscured margins are with difficulty seen; the surface congestion is more decided and gives rise to a "juicy" impression; the retinal veins, often only one division of them, are darker, more distended and more unevenly tortuous, indeed, decided tortuosity of the retinal veins, especially of one or two of the larger branches, may appear before any obscuration of the disk. At this stage, photometric examinations may give aid in diagnosis.

A swelling of at least 3 D. should exist before the name "choked disk" is permissible, but it is not worth while to enter into a discussion of the various aspects of neuritis or "choked disk." As Hughlings Jackson has said, there is one kind of optic neuritis from intracranial disease which may manifest itself under different appearances, sometimes with and sometimes without "swelling of the disk."

Ophthalmoscopic examination is not always made during the period of typical optic neuritis or choked disk; patients may come after the evidences of inflammation and œdema have begun to subside—at the period, in other words, when the veins grow less distended, new hemorrhages do not appear, previously obscured vessels reappear and the swollen nerve-head begins to be depressed and the grayish-red tint of the prominence becomes more uniformly gray and grows paler. The temporal edge of the disk is first to appear, and gradually the other margins emerge from the obscuration. Finally, all edges of the disks are clear, and the well-known symptoms of *post-papillitic atrophy* are present, quite distinguishable from either a *primary* or a *secondary atrophy* by the presence of the tissue which fills in the centre of the disk and obscures the lamina cribrosa so prominently visible at the bottom of the shallow cupped, primarily atrophic disks. Both sets of vessels, too, are contracted and streaked with infiltrated perivascular sheaths. Areas of retino-choroiditis and patches of white marking the spots of former hemorrhages are often apparent.

In rare instances a *second attack of optic neuritis* takes place. A good example of this I observed in the Orthopædic Hospital and reported with Dr. A. G. Thomson.[1] In this case the patient was trephined for the relief of the symptoms of a tumor believed to be situated in the right motor area. It was not possible, however, to remove the tumor, although great relief followed the trephining. Three and one-half months after operation the double optic neuritis had subsided and there was post-neuritic atrophy. One year later the patient returned with all the symptoms of brain tumor re-established (from which he had previously been entirely free), totally blind and with double optic neuritis, the apex of each swelling being 6 D., or as high as it had been before the original operation.

As may have been inferred, the tendency of optic neuritis or papillitis is to cause atrophy of the nerve, but optic neuritis may remain stationary for long periods of time and finally disappear without leaving a trace of its presence. Naturally, as Oppenheim points out, such a state of affairs could be expected only if the original disease subsides, or there is relief of intracranial pressure by trephining. Excep-

[1] Archives of Ophthalmology, xxiv. 1905.

tionally, however, as he notes, the original disease continues but the neuritis subsides.

In place of optic neuritis as a sign of brain tumor, *optic nerve atrophy* itself without indications of pre-existing neuritis may appear. This is particularly true in the case of basal tumors, for example of the hypophysis, and depends upon direct compression upon the chiasm, the optic nerve tracts or the optic nerves themselves. It may also be produced by bulging of the lateral ventricles and the pressure thus exerted by them. This is the so-called *secondary atrophy*. The color of the disk is gray and assumes a tint not unlike that of primary or progressive atrophy. More often the color of the disk is whiter than in gray atrophy. Both sets of vessels are contracted. This secondary atrophy must be distinguished from the consecutive or post-papillitic atrophy, to which reference has already been made. I suspect that in a certain number of cases there is a period of congestion of the disks preceding the atrophy, which may or may not have been observed.

In discussing the ocular symptoms of cerebellar tumor,[1] it was stated that the papillitis of intracranial tumor is sometimes unilateral and that where there is a one-sided optic neuritis, or a marked difference between the two sides, it is suggestive of the fact that the cerebrum is the seat of the growth, and on the whole in favor of the tumor being on the same side as the excess of neuritis. J. M. Martin's investigations on this subject are important and show that the seat of the lesion is probably on the side on which the optic neuritis is more marked in the proportion of 71 to 29. Although unilateral optic neuritis, or, more accurately, excess of neuritis on one side, occurs in tumors of the cerebellum, it is a much less common symptom than in the cerebral cases.

(*c*) Retinal Changes. A very interesting appearance is the so-called macular figure, in other words, a lesion simulating that seen in albuminuric retinitis. It is said to be more frequent in cerebellar growths, but has been observed a number of times with tumors having other situations. The most perfect figure of this kind which I have noted occurred with a subcortical tumor in the parieto-occipital region.

In thirty cases of tumor reported by Leslie Paton[2] these macular changes were noted five times, one frontal case, one parietal case, two cerebellar cases and one extracerebellar case. Kamplherstein found eight times in his two hundred cases of choked disk (one hundred and thirty-four of these were brain tumor cases) involvement of the macula, but only once a typical star figure, such as one sees in retinitis albuminurica. Therefore, the macular involvement is not always a star figure, due probably to œdematous infiltration, and is not necessarily associated with great depreciation of vision, but may be, as in Kamplherstein's seven other cases, composed of smaller and larger hemorrhages or irregular white plaques of exudation. Indeed, Bruns refers to these as a not uncommon development in the macula at the height of choked disk, and believes that the appearance there of yellowish-white and fatty degenerated spots intermixed with hemorrhages is of serious import. In a number of cases I have seen these macular exudates quite distinct from star-shaped œdematous areas, both with and without hemorrhages, and have studied them at the height of the choked disk as well as in its later stages, both in cerebellar and in cerebral tumors.

Other retinal changes have already been referred to, particularly areas of atrophy, marking the position of former hemorrhages, sclerotic patches in the retinal vessels, perivasculitis, pigment-heaping, which are in no sense significant of the growth itself but only of other ocular lesions which have accompanied it.

(*d*) Visual Acuteness. Optic neuritis or choked disk caused by cerebral growths is perfectly compatible with good acuteness of vision. Indeed, as has many times been pointed out, perfect vision, in so far as test-letter examination is concerned, may exist for long periods of time, although there is well-marked engorgement of the nerve-head, or all of the signs of papillitis. Even where the visual acuteness appears not to be normal, but is reduced, for example, to one-half or one-third, or even one-tenth of normal, it may often be raised nearly or quite to the normal standard if a suitable glass corrects any co-existing refractive error. A good example of this occurred recently in the University Hospital. A boy with moderate optic neuritis, probably the result of meningitis, following a fracture of the skull, apparently had a vision of only $\frac{6}{36}$, but as his eye was hyperopic 4 D. at the macula, this glass promptly raised his vision to $\frac{6}{9}$, in spite of the presence of 2 D. of neuritis. In other words, visual acuteness recorded without note of the refractive error and the effect of neutralizing lenses does not give a true indication of the real sharpness of sight.

An interesting fact often mentioned and again referred to by Leslie Paton is the rarity with which one finds optic neuritis or choked disk in eyes that are myopic. This accords exactly with my own experience, and in one notable instance with a myopia of 10 D., although all signs of brain tumor had been prominently present for nearly two years, there was no optic neuritis until ten days before the patient's death, when, preceded by marked venous engorgement, congestion œdema followed by rapid neuritis developed, so that the disks were swollen 2 or 3 D. at the end of that period. A not uninteresting research would be one which included a study of the exact refractive condition at the macula of eyes with optic neuritis associated with brain tumor, and of eyes exhibiting no neuritis, although other signs of cerebral neo-

[1] Loc. cit.

[2] Transactions Ophthalmological Society of the United Kingdom, xxv. 1905, p. 129.

plasm are present. It is possible that it might lead to an explanation of the lateness of the development of neuritis in certain cases, as for example in the one just mentioned.

Differences in the visual acuteness of the two eyes is not uncommon. The vision of one eye may be normal, while that of the other may be only one-half or one-third of normal. Usually this difference, if not caused by refractive error, depends upon the degree of the neuritis, or upon post-neuritic changes. A considerable atrophy of the nerve may exist in one eye and no apparent atrophy in the opposite eye, which possesses normal or nearly normal vision.

The relationship between the site of the tumor and the vision is discussed by Leslie Paton[1] in his important communication on optic neuritis in cerebral tumors. Of seven patients with frontal tumor, three retained normal visual acuteness during the whole course of the attack. In one, the sight at one period was reduced to two-sevenths of normal, but subsequently recovered. In three the sight of the eye on the side corresponding to the tumor was defective, while the eye was left in a normal condition on the other side. In ten cases of parietal tumor he records four as having retained good sight, three as having suffered from defective sight during the height of the attack, with subsequent recovery, while in three the sight was entirely lost, with no recovery. These recoveries were the result of the operations which were performed for the relief of the symptoms which the tumor produced, to which reference will be made in a later paragraph. In contrast to this, it may be mentioned that Paton records eleven cerebellar cases, and only one showed no marked loss of sight during the course of the neuritis.

Temporary amaurosis in brain tumor is a sign of decided importance. Although the visual acuteness in the presence of choked disk may be entirely normal, or reach close to the normal standard, the patient may have periods of temporary amaurosis which last from a few minutes to a few hours, and, it is said, may continue for several days, to be followed by a restoration of the visual power to that which existed prior to their occurrence. In a patient recently under my observation in Dr. Frazier's wards these amaurotic periods first called the patient's attention to his eyes, and led to their examination and the discovery of papillitis. In this case the periods of obscuration lasted usually from ten to fifteen minutes, according to the patient's statement. Those which I witnessed were not quite so long—five to six minutes. Form-sense was obliterated but light-sense still remained. It would seem that these amaurotic attacks are the result not of the neuritis but of compression of the chiasm by the bulged floor of the third ventricle.

Michel has stated that the amaurosis is related to pressure from the third ventricle, if it appears quickly in both eyes, or rapidly in one eye after the other. The patient before referred to experienced the most marked attacks in the left eye, that is, on the side on which the tumor existed. He declared that occasionally the amaurosis was unilateral; this statement, I did not substantiate by personal observation. There was however, an appreciable difference in time between the development of the attacks, and the left eye was the first to suffer.

Paton's observations lead him to say that transient attacks of blindness may last for periods varying from a few seconds to half an hour. The symptom was noted twelve times in his series: six of these were cerebellar cases, three frontal, two parietal and one pontine. In another series of cases (thirty-eight) he found this symptom mentioned in four, all cerebellar tumors, and suggests that the condition may be due to interference with the blood supply of the occipital lobe, but because increased headache and attacks of giddiness accompany the symptom there is evident pointing to an increase in intracranial pressure as its most prominent etiological factor.

Mr. Gunn, discussing this matter, maintains that the occurrence of complete temporary loss of sight in one or both eyes under these conditions cannot be explained by a local effect upon the sight-centre. It must be due to sudden increase in intracranial tension and loss of function by pressure exerted on the optic nerve fibres.

Amblyopia and blindness without eye-ground changes have been observed by Curschmann, Gerhardt and others, and have been attributed to the bulging forward of the floor of the third ventricle and pressure upon the chiasm.

(*e*) The Effect of Operation on Optic Neuritis or Papillitis. It is not the purpose of the present paper to discuss in detail the various theories which have been advanced to explain the development of papillitis or choked disk. In general terms it may be stated that a certain number of cases of papillitis represent a true engorgement œdema, and that the evidence of inflammation, at least in any decided degree, is lacking, while in others the inflammatory signs are decided. Where engorgement œdema is the marked feature the ophthalmoscope reveals the typical picture of choked disk. In other cases, however, the elevation of the disk is less decided and the inflammatory condition predominates, the process extending to the retina, where exudates and hemorrhages are visible; in other words, an inflammatory optic neuritis is present. Kampherstein, as the result of his own work and the review of the observations of others, declares that in our present state of knowledge there can be no absolute adherence to the mechanical theory, especially championed by Schmidt-Rimpler and Manz, a theory which is often known as the lymph-space theory; neither is it possible to explain all cases by assuming a descending inflammation which passes from the lesion in the brain to the end of the optic nerve, as

[1] Transactions Ophthalmological Society of the United Kingdom, xxv. 1905, p. 136.

B. J. C. D.

many for example, Gowers, are inclined to believe, nor by adopting the theory that the papillitis is not the product of an œdema but is an inflammatory affection in the sense that the fluid distends the sheath of the optic nerve and possesses an irritative quality. He does believe that the condition often is best explained by a preceding œdema of the brain extending through the optic nerve to the lamina cribrosa, and thus causing choking of the nerve-head. As, however, the percentage of eyes in which there is neither œdema of the nerve nor distention of the interspace is a large one, it is impossible to accept alone the mechanical theory, and raised pressure sufficiently maintained must, in a certain number of instances at least, be the direct cause of choked disk.

The important fact remains, no matter which one of the theories is adopted, that there may be a subsidence of optic neuritis after operation undertaken with a view to the removal of an intracranial tumor, even if the tumor is not removed. In other words, palliative trephining is of the utmost importance and is an operation which should be practised early. Much has been written upon this subject, notably by Horsley, Bruns, Erb, Taylor, Saenger and others, but in many respects the most satisfactory study of its great advantages, both when the tumor is removed and when it is not removed, is by Leslie Paton.[1] His material consisted of thirty cases in which he was able to trace the changes in the eye conditions subsequent to operation as they occurred in the National Hospital in Queen Square. In general terms, useful vision was saved in 22 out of 30 cases, and in 18 the vision at the time the last record was made was as good as it was before the operation. It is not quite clear from the records just how often the entire tumor was removed, but apparently in 18 of the cases, while in 5 of them the operation consisted either in simple trephining or in trephining with an effort, but an unsuccessful one, to find the tumor. In 7 of them it is not definitely stated whether the growth was removed or not. All of the operations were done in two stages, the first, consisting in removal of the bone and, if the intradural tension was high, incision of the dura, and the second one a week later, in which the tumor itself was removed if possible. Some examinations were made between the first and second stages with the result that little measurable alteration could be seen in the disks. Usually, within a week or a fortnight after the second operation, there was definite subsidence of the swelling, and this subsidence continued so that at the end of two months in most cases the swelling had disappeared.

I have studied a number of cases in the surgical practice of Dr. W. W. Keen, Dr. Edward Martin and Dr. Charles H. Frazier, and in general terms I can confirm the results recorded by Paton. My experience has been somewhat as follows: Usually there is no distinct change in the swollen nerve-head after trephining in which the dura has been opened, or after the removal of a tumor, until the tenth to the fourteenth day.[1]

After this period there is gradual subsidence of the neuritis, from six weeks to two months being required for its complete disappearance. The ultimate vision may be *(a)* better than that which existed prior to the operation; *(b)* equal to that which existed prior to the operation; *(c)* worse than that which existed prior to the operation. Sometimes total blindness results. In the cases with preservation of vision, either as good as or better than that which the patient possessed before the operation, the sight may be better in one eye than the other, or exceedingly defective in one eye and good in the other, or one eye may be blind and the other retain or regain excellent vision.

Naturally, the most satisfactory results follow the reduction of great intracranial pressure, provided the papillitis or choked disk has not so long existed that it has already destroyed the optic nerve fibres. Three cases illustrating the effect of operation on papillitis may be quoted:

1. Sarcoma of cerebellum; choked disks each eye 7 D. Tumor removed by Dr. Frazier. No change noted (daily examinations) until the fourteenth day after operation, when apex of disks was 6 D. During the next fourteen days there was rapid decline in the swelling, so that twenty-eight days after operation it was only 3 D., and the edges of the disks were beginning to appear. Within the next month all neuritis disappeared and post-papillitic atrophy was present. Blindness was complete, but vision had equalled only light perception prior to operation.

2. Cerebral tumor; choked disks each eye, 6 D. in right and 4 D. in left; vision, $\frac{6}{12}$. Craniectomy and opening dura by Dr. Frazier. First distinct change noted in disk, thirteen days after operation, followed by rapid subsidence, ultimate vision, $\frac{6}{12}$.

3. Cerebral tumor (cerebellar?); double choked disk, right + 11 D., left + 9 D. Vision: O. D., $\frac{6}{15}$; O. S., blind. Trephining by Dr. Frazier. No change in disk until the eleventh day, then right, + 10 D., left + 10 D., showing slight increase in swelling on the blind side. Swelling then remained stationary for nine days, when rapid subsidence began, and at the end of six weeks practically all swelling had subsided. Vision: O. D., $\frac{6}{9}$; O. S., blind.

In a certain number of cases during the first day or two after trephining there may be a slight increase in neuritis, or, more accurately, a slight increase in œdema, associated with fresh hemorrhages. This is apparently of no importance, as the added œdema and fresh hemorrhages disappear in the subsequent general subsidence of the swelling.

[1] Transactions Ophthalmological Society of the United Kingdom, xxv. 1905, p. 129.

[1] Dr. Spiller informs me that marked subsidence of engorgement œdema has been seen at the end of forty-eight hours. I have not observed such an early change in any case.

In some of these cases there are marked degenerative changes in the retinal vessels. An illustrative case is the following: Tumor of cerebrum; double choked disks: right, + 4 D.; left, + 5.50. Removal of the tumor by Dr. Frazier in two operations four days apart. Five days later increased neuritis and many fresh hemorrhages; marked sclerosis of retinal vessels. Patient had widespread arteriosclerosis.

Mr. Paton has also noticed in four of his cases fresh hemorrhages after operation, usually within ten days after removal of the growth, and in one case a month after operation. He has also in two cases observed a slight recrudescence of the swelling occurring usually within the first month. That a second attack of optic neuritis may occur, I have shown by a case already reported.

A matter of some importance which I have noted on several occasions is temporary depreciation of vision within the first week after the operation, probably due to shock, perhaps to hemorrhage, and which is apparently of no importance in the subsequent restoration, or rather preservation, of vision, provided the primary vision has been good and the neuritis of comparatively short duration. In cases, however, in which very little vision exists prior to the trephining, for example, a vision reduced to hand movements, or even light perception only, this may rapidly disappear after trephining, especially if there has been much hemorrhage. For example, in three recent cases, namely, a tumor of the lobe of the cerebellum, a growth of the pontial angle, and a cyst of the left lobe of the cerebellum, all young women, vision had been reduced prior to operation to hand movements in two and to the ability to distinguish very large letters held close to the eye in a third, were completely blind, even to the abolition of light perception within the first week after operation, although in each instance the surgical success was a brilliant one.

In the discussion of Mr. Paton's paper, before referred to, Risien Russell stated that there was no doubt in his mind as to the value of trephining with the object of saving sight in cases of intracranial tumor, and that he never hesitated to recommend the operation, even when there was no chance of either localizing the growth or of removing it because the relief of intracranial pressure alone might be the means of preserving vision. He was quite sure, however, that it was necessary not merely to remove a piece of bone, but that the dura mater should also be opened. That palliative trephining for the sake of saving sight is a proper operation is abundantly confirmed by my own experience, and the earlier it is performed the better will be the patient's chances of retaining or regaining his vision.

Significance of Optic Neuritis. Although the presence of bilateral papillitis is highly significant of cerebral tumor, of itself it possesses no distinct localizing importance. In this connection, however, it is proper to quote from J. M. Martin's careful analysis of 601 brain tumors that optic neuritis is constantly present in cases of tumor of the corpora quadrigemina, that it is present in about 90 per cent. of cases of tumor of the cerebellum and posterior part of the cerebrum, and that it is absent in nearly two-thirds of the cases of tumor of the pons and medulla and of the corpus callosum. Unilateral optic neuritis, or decided excess of neuritis in one eye, indicates, as already noted, that the tumor is on this side. Martin shows that the seat of the lesion is probably on the side on which the optic neuritis is more marked in the proportion of 71 to 29. The assertion of some observers that one-sided optic neuritis indicates a tumor on the corresponding side situated in the temporal lobes is emphatically denied by Bruns. That temporary amaurosis may have a localizing significance and indicate a tumor of the occipital lobe, as stated by Bruns, is doubted by Oppenheim, and is contrary to my own experience. Paton found the symptom most often in cerebellar tumors. In the most marked case I have seen the growth was in the left motor area. No positive conclusions as to the size of the tumor can be drawn from the intensity of the choking of the disk, because although great engorgement edema may be caused by a large tumor, the reverse is sometimes true, and a small tumor may be associated with great swelling of the nerve-head. Sudden increase in the neuritis or engorgement may be suggestive of sudden increase in the size of the lesion or of the intracranial pressure.

ANOMALIES OF THE VISUAL FIELD.

Changes in the visual field in optic neuritis are not uncommon. Thus, in Kampherstein's list of 200 cases some form of alteration was present in all but 17 cases, and 16 of these were quite recent ones. There may be irregular and concentric contraction of the visual field, increase in the size of the normal blind spot, which becomes correspondingly great in conformity with the amount of swelling, the formation of an abnormal blind spot or scotoma due to involvement of the axial fibres, and sometimes to destruction of the ganglion cells, the absence of half of the visual field (hemianopsia) when the intracranial tumor which may have been the cause of the papillitis is so situated as to produce these phenomena. Finally, there may be defective color perception which may exist when there is no change in the central vision and no limitation of the form field. In one of Kampherstein's cases there was total color blindness. In this case, however, there was also contraction of the visual field.

Of more importance than any of the changes in the visual field are the various types of hemianopsia. Naturally, in bitemporal hemianopsia, sometimes called the localizing form of hemianopsia, it is usually fair to assume that there is obstruction in the conductivity of the crossed fasciculi, the non-crossed fasciculi remaining intact. Thus, in a recent

case of typical bitemporal hemianopsia, which I studied in the practice of Drs. Mills and Tyson, a metastasis from mammary carcinoma was so situated that the optic chiasm was invaded and pressed by it. It is, therefore, a well-known sign of basal tumors and of tumors of the pituitary body, but it should be remembered that a growth at a distance from the chiasm may occasion a field simulating a bitemporal hemianopsia. For example, as Swanzy, Gowers and others point out, a tumor of the cerebellum by closure of the aqueduct of Sylvius may produce internal hydrocephalus and thus exert pressure on the chiasm. So far as I am aware, bitemporal hemianopsia has never been observed, as has cortical hemianopsia, as a distinct symptom. Destruction of the retinal ganglion cells in connection with papillitis may give rise to fields of vision which closely simulate hemianopsia.

A symptom of some importance which may be mentioned here is the so-called *chiasmal central amblyopia*, in which, according to Nettleship, "the loss of the central field in the earlier stages is more rapidly defined than in tobacco amblyopia, and the symmetry less precise both in time and degree than in the latter disease." In one such case the chiasm was involved by a cyst.

Tumors which press upon the optic tract or the visual pathway posterior to the optic chiasm naturally produce homonymous hemianopsia, which, hence, is a symptom of great importance in locating the tumor, but which is not now under discussion. Homonymous hemianopsia, however, may be a distinct symptom and not give a true indication of the situation of the growth. In a very remarkable case, which I observed in the practice of Dr. H. C. Wood, and which has been reported by him, a large growth existed in the temporo-sphenoidal lobe, but what at that time was considered the most important localizing sign, namely, a lateral hemianopsia, was caused by a small cyst in the cuneus, not connected with the growth, the situation of which, indeed, was unsuspected until an autopsy revealed its presence.

Although anomalies of the ocular muscles and the movements of the eyeballs constitute an important part of the symptomatology of certain brain tumors, their consideration is omitted from the present paper because in so far as they assist in localization they are discussed elsewhere by Drs. Mills and Weisenburg.

There are no characteristic pupil-phenomena, and, as Kampherstein has shown, in the majority of cases of choked disk the pupil reaction is normal. Although with complete loss of vision due to atrophy the pupil is usually immobile to light impulse, it is not invariably so, as Kampherstein records normal reaction in five cases of total blindness, in three of which optic nerve atrophy was present. Such cases he regards as demonstrating how resisting are the fibres of the optic nerve which convey the light reflex, provided the degenerative process is local in the nerve and the central fibres are not destroyed.

REMARKS UPON THE SURGICAL ASPECTS OF OPERABLE TUMORS OF THE CEREBRUM.[1]

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During the past decade there has been a renewal or revival of interest in the surgical aspects of tumors of the brain, chiefly because of the frequent failure even to find the tumor the earlier attempts were attended with disheartening results and there was a period in which surgical therapy was abandoned almost as a means of affording relief for patients affected with brain tumors. At the present time, however, there is a widespread activity in this field of surgery and the many problems relating thereto are being carefully studied and freely discussed. As a result of this renewed activity the surgery of brain tumors is established upon a much more exact basis, the indications for or against surgical intervention are more clearly defined, the methods of dealing with the great variety of conditions, at first somewhat perplexing, are more clearly understood, and the details in technique have been so elaborated that the operation can now be performed with but slight risk to the patient's life and the prospects of improvement or recovery are very much greater. We have still, however, much to learn, and the results which have been attained thus far are still far from ideal. Dr. Mills has dealt in his paper with what might be said to be the most important phase of the whole subject, namely, the diagnosis, since it is only by the early recognition of the presence of a tumor that we can hope to increase the percentage of operable tumors and thereby the percentage of cures. This paper will be devoted chiefly to a discussion of questions pertaining to the technique, and the views expressed are the result of my observations in a large number of cases which, especially through the courtesy of Dr. Charles K. Mills and Dr. William G. Spiller, I have operated upon at the University Hospital during the past five years.

[1] This paper was prepared as a sequel to the paper of Dr. Charles K. Mills upon "The Focal Diagnosis of Operable Tumors of the Cerebrum," published in this issue of the Bulletin.

The Operability of Tumors. Walton and Paul[1] made a study of the clinical and postmortem records of 424 cases, many of which were observed by themselves or their immediate colleagues. They divided their cases into (1) operable tumors, under which head they include the primary, accessible, well-defined tumors which may be removed without cutting the brain tissue, springing in the great majority of cases from the dura; (2) inoperable tumors, including those involving deep-seated structures, the basal ganglia, the pituitary body or the middle lobe of the cerebellum, extensive infiltrating gliomata and most cases of multiple growth and metastasis; and (3) doubtful cases, including gliomata and non-encapsulated sarcomata in accessible regions, and many subtentorial tumors and cysts which can simply be evacuated. Of the four hundred and twenty-four cases, they classed thirty, or 7 per cent., as operable; three hundred and thirty-eight, or 80 per cent., as inoperable; and fifty-six, or 13 per cent., as doubtful, the combination of operable and possibly operable reaching to 20 per cent. By eliminating cases in which metastasis or infection was present and cases without diagnostic symptoms, the number of operable cases was reduced to fourteen, or 3.3 per cent., and the doubtful to thirty-four, or 80 per cent.

The term operable would seem to be made practically synonymous with curable by Walton and Paul; it should have a wider significance than this, that which is partly given to it under their designation of doubtful cases. Any case of brain tumor which can be reached and wholly or partially removed with subsequent benefit to the patient should be regarded as operable, remembering that we are in the presence of a disease almost absolutely fatal without operation.

A few sources of fallacy may be present in statistical studies like those of Walton and Paul. In the first place their conclusions are drawn from a study of cases which came to autopsy. No criticism is to be made upon this fact, as it is only by a study of such cases, and those in which operation has been actually performed and the tumors reached, that we can get positive data for our guidance; but the size and radiations of tumors found at necropsies are different in many cases from their size and extensions at the time when operation should be taken into most favorable consideration. Again and again I have seen on the postmortem table a brain tumor which would have been inoperable a short time before death, but which might have been entirely removed a few months or a year or two previous. This is true especially of dural tumors which have grown and destroyed brain tissue by invasion and obliteration of vessels, and also to a less extent of infiltrating tumors.

In rare cases small tumors of the middle lobe of the cerebellum, if operated sufficiently early, might be removed, although not after they have extended so as to form connections with inaccessible regions. The period of the development of the tumor has therefore considerable to do with its operability wherever situated.

Distinct advantage may result to the patient, as I have seen, from the evacuation of cerebral cysts, although such benefit is not always derived.

A point of much practical importance in the settlement of the question of the operability of a brain tumor, or rather of the advisability of operating, is that which is based upon the question of what the operation is expected to accomplish. Operation should be advised in every case in which relief from suffering for any considerable period can be secured. In a few cases, tumors of the brain can be so completely removed that the patient may be regarded as cured; in a few others the growth can be removed in whole or in part with chances in favor of its return, but with great temporary benefit to the patient; in a third class of cases operations beneficial in relieving the painful and distressing symptoms of the disease, although the growth cannot be removed at all. Cerebral tension and irritation are diminished in this class of cases, and blindness from optic neuritis is often prevented, relieved, or deferred.

Of the operable cases the most accessible, and therefore, those which promise most success, are the tumors which arise and develop on the lateral aspect of the cerebral hemisphere the growths with which this paper is particularly concerned.

So much as has been said thus far as to the operability of tumors has had to do chiefly with their accessibility and inaccessibility. A word or two might be said with reference to the nature of the growth. If the tumor is found to be very vascular and of the infiltrating type, it is very questionable to my mind as to whether any attempt whatsoever should be made to extirpate it. If the tumor is not encapsulated, it is impossible to tell how much tissue should be removed and there is always a likelihood of a portion of the tumor being left behind. In the performance of operations for the removal of malignant lesions in any part of the body, it is a well-known clinical fact that if the operation is imperfectly performed the tumor begins to grow at a very much more rapid rate than prior to operative interference. In addition to this the hemorrhage which occurs upon attempts at removal of very vascular growths is most profuse and of such a character that it is very difficult and sometimes impossible to control unless one resorts to so formal a procedure as closure of the carotid arteries. This of itself may determine a fatal issue. For these reasons, therefore, I am disposed to include among the inoperable class of tumors not only those which are found to be inaccessible but also those which are of the type already described. No matter which operation is performed the condition must be regarded as an incurable

[1] G. L. Walton and W. E. Paul, Journal of Nervous and Mental Disease, vol. xxxii., August, 1905.

one and there is no question but that the patient will enjoy a period of relief quite as long if not longer, and quite as free from distressing and annoying symptoms, when a simple decompressive operation is performed. Furthermore, the chances of recovery from the immediate effects of the operation are very much greater, of course, after the palliative than after the radical procedure. The mortality after simple decompressive operations in which no attempt is made to remove the tumor should be very low.

Technique of Craniotomies. In the great majority of our cases the following technique was observed: the day before the operation, the patient's head having been shaved, the shape of the flap to be reflected was carefully mapped out by certain craniometric lines, usually the Anderson-Makin lines, at first with an aniline pencil and then with a stick of nitrate of silver. In the course of two hours the nitrate of silver lines will be sufficiently fixed to prevent their being rubbed out during the disinfection of the scalp. A word or two might be said at this juncture as to the desirability of mapping out a flap according to a reasonably accurate craniometric method. I have heard it said that it is entirely unnecessary, for example, to determine the position of the central fissure with relation to the scalp before operating for the purpose of exposing the motor area; that with a little experience one should be able at a glance to tell in a general way the position of the fissure. One has but to familiarize himself with the marked variations in the position of the fissure in heads of different shapes to realize how impossible this would be. If we turn, for example, to the admirable studies of Froriep it will be seen how variable the position of the fissure is in relation to the external auditory meatus. I have selected the ear or the external auditory meatus as an example, because the available illustrations demonstrate this point. In some cases the fissure is entirely behind the line of the external auditory meatus, in some the fissure crosses it and in some it is almost in front of it. In answer to this argument one might say that if a large enough area is exposed, if the flap is big enough, one can be sure of exposing the entire motor area. That is perfectly true, but there are many reasons why an unnecessarily large flap should not be made. The motor flap, which I am in the habit of making, measures from three and one-half to four inches in width; if because of uncertainty as to the precise position of the fissure an inch and one-half or two inches were added to the width, which is a reasonable allowance to make, the flap would measure five and one-half to six inches in width. While it is quite possible to reflect a flap of these dimensions, and even a larger one if need be, such a procedure is quite as unjustifiable as the making of an incision in the abdominal wall six inches long, when one three inches long would answer the purpose quite as well.

There are other reasons, however, for determining before the operation the position of the region which it is desired to expose. If this precaution is not taken it is quite possible that the operator might fail to expose the lesion. Tumors are not always situated entirely within the regions to which the symptoms are referred. A tumor might only encroach but a little upon the motor area and yet give rise to motor symptoms. If the opening were half an inch or an inch too far backward or forward it might fail altogether to expose the tumor.

To return from this divergence to the technique, the patient is placed upon the table, secured in the manner to be described, the anæsthetic, ether, is then administered by the assistant anæsthetist. The chief anæsthetist disinfects his hands as thoroughly as though he were going to participate in the operation, puts on a sterile gown and gloves and does not take charge of the anæsthetic until the patient's scalp has been disinfected and the operation is about to begin. These regulations regarding the anæsthetist are really important, though seemingly insignificant, because the hands of the anæsthetizer are so near the field of operation that there is always the possibility of their coming in contact with the instruments or objects that may be employed during the course of the operation. Prior to the beginning of the anæsthetic an observation is made of the blood pressure, and this is repeated at intervals of five minutes or oftener. The table is now elevated, and as the incision is made the assistant makes firm pressure at the base and sides of the flap for the purpose of controlling bleeding until a few hæmostats may be applied. A small opening is made in the skull with the burr or chisel and the bone divided with the spiral steotome. In some cases, particularly if the bone is unusually thick, the base of the flap or the bridge of bone between the two extremities of the incision is partially divided with a Gigli saw, but in the majority of cases this bridge of bone is broken across by elevating the flap. When this has been accomplished a piece of gauze is wrapped around the osteoplastic flap and allowed to remain there until the end of the operation. I insist upon this because of the possibility of the bone in the flap being denuded of its periosteum and the overlying scalp, thus depriving the bone of its blood supply and necessitating its removal. The dura is then inspected, the presence or absence of adhesions and of pulsation of the brain noted. The absence of pulsation is always indicative of increased tension, which may be due to a large cyst, tumor, abscess or internal hydrocephalus. After the dura flap is reflected, by making an incision about one quarter of an inch from the margin of the bone, the appearance and consistency of the cortex is noted. A rapid survey is made of the exposed field for any pathological condition that may be detected by sight or by delicate palpation; there may be an increased consistency of the cerebral tissue, as in the presence of a tumor, or diminished consistency and a sense of fluctuation, as in the

presence of a large cyst or an internal hydrocephalus; abnormally dilated veins or opaque milky streaks along the course of the pial vessels or any variation from the appearance of normal brain tissue should be noted.

It is important to note whether the brain bulges through the opening once the dura is removed. Bulging of the brain may sometimes be the most troublesome feature of the operation. We should distinguish between what might be called "initial" bulging, or that which occurs immediately after reflection of the dura, and "consecutive" bulging, or that which manifests itself during subsequent exploratory manœuvres. The initial bulging is indicative of the presence of considerable increase in the intracranial tension, such as might be due to internal hydrocephalus or the presence of a large tumor. This however, is not invariably the case; a tumor may be present and yet there may be little or no "initial" bulging. To illustrate this I could cite the case of a cortical sarcoma of moderate dimensions and another of a large subcortical tumor in neither of which was there any initial or consecutive bulging. Naturally, however, the character of the tumor has to be taken into account; thus a very vascular sarcoma would be more apt to bulge through the opening than a gumma. The release of pressure from a growth abounding in large vascular channels would result in a reactionary dilatation, more particularly of the venous channels, and this in turn might be followed by such circulatory disturbances as would readily lead to cerebral œdema. During the course of the exploratory manipulations the brain may bulge to an inconsiderable degree through the opening, even when the tumor is not found, or if present, is not situated at or beneath the area exposed. This consecutive bulging is due no doubt to the traumatism of a greater or less degree inflicted by the exploratory measures and to the exposure of the brain surface to the injurious influence of a comparatively low temperature. The swelling and bulging under the circumstances is no doubt due to œdema; this, as Cannon pointed out in connection with the secondary increase of intracranial pressure in head injuries, is the result not of any increase of blood pressure but of certain chemical changes in the brain substance itself, whereby the osmotic pressure is so increased that the brain becomes rapidly œdematous.

The subsequent steps vary according to a number of circumstances. If nothing abnormal has been found by this preliminary examination the question of further exploration is then considered. (This is a matter of so much importance that it will be treated more at length under a separate heading.) This consists in either an incision into the cortex, where there is an evident increase in the consistency of the brain or in the introduction of a special exploratory canula where there is reason to suspect a cyst, abscess or internal hydrocephalus. When the exploration is concluded and the lesion, if found, appropriately treated, preparations are made to close the wound. Hemorrhage from every source should be checked as far as possible: from the cerebral veins whenever possible by ligation, otherwise by tamponade, and from the bone by Horsley's wax. There will always be a certain amount of bleeding or oozing, and to prevent the formation of a hæmatoma beneath the flap adequate drainage must be provided. The flap is replaced and the edges of the wound united by interrupted silkworm-gut sutures. These sutures, if properly introduced, will control bleeding from vessels in the scalp, thus providing the necessity of applying ligatures. Drainage is provided by introducing a strip of rubber tissue through two counteropenings, one just in front and the other just behind the flap. Whatever oozing there may be will be spontaneously arrested within twenty-four hours. The drainage may be removed then or at the end of the second day, when the stitches are removed and a collodion dressing applied. The patient is not confined to bed more than three or four days unless the operation has been an unusually severe one.

Subcortical Growths and the Limits of Exploration. One of the most difficult questions, and one which must be decided during the course of an operation for the exposure of a tumor, is the question of exploration for subcortical growths. Given a case in which, when the dura is reflected, the tumor is not visible to the naked eye, should the case be regarded as inoperable and an attempt to find the growth be abandoned, or should we proceed to further exploration with the hope of exposing and removing a subcortical growth Referring again to the statistics of Walton and Paul it would appear that the field for surgical intervention in brain tumors was a very limited one. According to Walton and Paul the tumors, which were operable, took their origin from the dura itself or were purely cortical tumors; in either instance they were visible to the eye of the surgeon as soon as the dural flap was reflected.

Of the tumors, which were not in either of these positions, the majority were so situated that they would not have been exposed by the usual exploratory incision or puncture that is made in the cortex. Codman (*Boston Medical and Surgical Journal*, July 20, 1095), after reviewing the records of operations for brain tumors, even goes so far as to suggest that we should be satisfied in every case with a purely palliative operation. An opinion so radical as this should not for a minute be entertained. I would advocate an exploratory incision, one or more, to the depth of at least one centimetre in every case in which the tumor does not appear in the cortex. Such a procedure is in itself comparatively free from danger, and if, from conservative estimates, there is but one chance in fifteen or even twenty of finding the tumor, the patient should be given the benefit of this chance. I know of one case in which the operator, failing to find

a cortical growth, declined to search for the tumor. The patient died shortly after the operation and a small, quite operable growth was found just beneath the cortex, so near the surface in fact that it would have been exposed by a very trivial incision. If a tumor has been accurately localized and the flap carefully mapped out we can be reasonably sure that it is situated in that portion of the brain that lies within the margins of the opening and should not hesitate to make one, two or more exploratory incisions in the cortex. To abandon altogether, as Codman suggests, what might be called the radical operation for the palliative one, would, I believe, be a retrograde step in the development of cranial surgery. There are certain cases in which it is possible beforehand to determine the precise position of the tumor, or in which the tumor is believed to be inaccessible, when no other course may be left to the operator than to perform a palliative or decompressive operation, but in all cases an attempt should be made to expose the tumor. A flap should be reflected in the region, in which it is believed to be situated, and an exploratory incision should be made in the cortex if the tumor be not visible upon the surface.

Anæsthesia. All the operations, which I have performed, were carried out under general anæsthesia and in every instance ether was the anæsthetic. Theoretically, chloroform might be preferred because, by lowering blood pressure, it might diminish the amount of bleeding, but its depressing effect upon the circulatory apparatus should of itself constitute not only a serious objection but a positive contraindication. In many cases of brain tumor, particularly those large enough to increase intracranial tension, disturbances of the cardiac and respiratory mechanism during the course of or immediately after the operation are not uncommon accidents. It is most important, therefore, that no drug be used which has a distinctly depressing effect upon either of these vital functions. For this reason, I have preferred not to use morphine-scopolamine anæsthesia. An hypodermic injection of one-sixth of a grain of morphine may be given fifteen minutes before beginning the administration of the anæsthetic, and there are no objections, so far as I know, to using ethyl chloride preliminary to the ether. Whatever may be the advantages in other operations of inducing narcosis with nitrous oxide, it should not be used in operations upon a patient with brain tumor. In the case of very vascular tumors and when there is much intracranial tension the veins are already much engorged; the intense cyanosis attending administration of nitrous oxide would cause still greater distention of the venous channels, so much so as to seriously interfere with the circulation of the brain. Of equal importance with the selection of an anæsthetic is the selection of an anæsthetizer. Except in cases of emergency the administration of the anæsthetic should not be entrusted to any but experienced hands. We are dealing with a class of patients who, as a rule, are not the best subjects for operative intervention, and who, therefore, demand the attention of a reliable anæsthetist. The condition of the patient must be watched with the greatest vigilance throughout the operation, and the operator himself should feel such absolute confidence in his anæsthetizer that his attention need not be distracted at any time from the field of operation. Whatever there is to be said of the desirability of having a regular anæsthetizer attached to operative clinics may be said with even greater force when the operation is to be performed upon the cranial cavity.

Position of the Patient. As a means of controlling hemorrhage, even though to a very slight degree, it is advisable to operate with the head of the patient somewhat elevated. In order that the patient may not slip down on the table during the progress of the operation, the patient is strapped to the table by a web belt which is passed under the table and over the patient's legs just below the knees. The table is then raised to an angle of thirty-five degrees. I have found it convenient in all operations upon the head to use a head rest which is especially useful in operations upon the posterior portion of the skull. All the necessary manipulations on the part of the operator and his assistants may be carried out with very much greater freedom, when the head projects on this rest beyond the edge of the table.

Hemorrhage. Considerable attention has been paid to the effect of hemorrhage during the course of operations upon the cranial cavity. As a rule, the amount of blood which escapes from the wound in the scalp and cranium is not sufficient to have any deleterious effect. Rubber tubing or inflatable tubing may be applied around the head as tourniquets, but neither of these have proven satisfactory in my earlier operations and I have come to depend solely upon the use of hæmostatic forceps. While the scalp incision is being made and the section made in the bone the assistants should be instructed to make pressure with gauze pads at the base and around the margins of the wound, since by this simple precaution a considerable amount of the hemorrhage may be controlled. Dr. Nicholson has had manufactured for his own use a set of hæmostatic forceps (Fig. 1), with broad blades, so

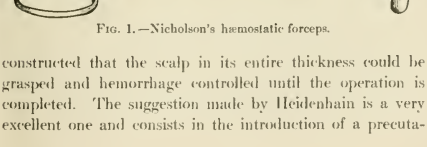


Fig. 1.—Nicholson's hæmostatic forceps.

constructed that the scalp in its entire thickness could be grasped and hemorrhage controlled until the operation is completed. The suggestion made by Heidenhain is a very excellent one and consists in the introduction of a precuta-

neous ligature through the entire thickness of the scalp surrounding the area in which the flap is to be made. I have never used this method myself, but in a letter recently received from Theodor Kocher, of Berne, he refers to Heidenhain's method as very efficacious.

So much for hemorrhage from the scalp; hemorrhage from the diploic sinuses may be satisfactorily controlled by plugging the sinuses with Horsley's wax. When engaged in the removal of a vascular tumor hemorrhage is very profuse and often alarming. It is a question whether any attempt should be made to remove these very vascular and usually infiltrating growths when of large dimensions; the immediate danger to life is great and the inability to determine precisely the limitations of the growth leave one always in doubt as to whether the tumor has been entirely removed. These are cases in which we should be satisfied with such palliative measures as can be derived from a decompressive operation.

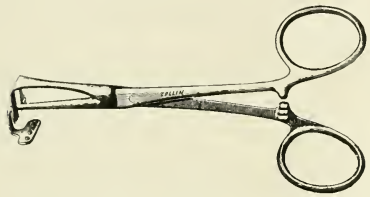


Fig. 2.—Howzel's hæmostatic forceps. (From Marion's Chirurgie de Système Nerveux.)

However, when the attempt has been made and the bleeding is profuse but two courses are open, gauze tamponade or temporary closure of one or both carotid arteries. Crile, to whom we are indebted for this suggestion, performed this preliminary operation in a series of operations without any serious ill effects. It seemed to me that if as in Crile's hands the operation were entirely free from danger a very important contribution had been made to the technique of cerebral surgery. Unfortunately, however, the danger of cerebral thrombosis resulting in death or in a hemiplegia is not an imaginary one, after ligature of one or the other carotid arteries, nor is it after only temporary closure. Unfortunately, too, closure of the carotids does not control hemorrhage entirely, the venous hemorrhage which is often the most troublesome is little, if any, affected. My own experience has been limited to six cases, two of which were excisions of the superior maxillary bone, the others brain operations, but from this limited experience, I should say that we should resort to this operation only in the most extreme cases and then apply it to one but not to both common carotid arteries. If copious hemorrhage is anticipated it is a good plan to expose the artery on the affected side as a preliminary measure, so that if the emergency arises a clamp may be applied immediately. Whether or not the patient is suffering any ill effects from hemorrhage, during the course of the operation, may be determined by observing the blood pressure. The sudden withdrawal of a large amount of blood from the system will have a deleterious effect by disturbing both directly and indirectly the circulatory apparatus. The latter may be detected by noting the condition of the blood pressure; if hemorrhage has been profuse and the blood pressure is falling, steps should be taken at once to replace the amount of circulatory fluid lost either with normal saline solution or a 1:50,000, adrenalin-saline solution. If the blood pressure has fallen but little the plain saline solution will suffice as a rule to restore the circulatory apparatus to its normal state; in cases, however, where the blood pressure is rapidly falling and signs of shock are impending adrenalin should be added.

Apart from the effects of hemorrhage upon the patient's general condition Dr. de Schweinitz has called my attention to the fact that in certain instances, as in a case recently operated upon, the choked disk, although it may eventually subside, may be increased somewhat after the operation. This he attributes to the effect of hemorrhage.

Observations upon the Blood Pressure. It has been our custom in all cranial operations to have observations made upon the state of the blood pressure with the Stanton modification of the Riva-Rocci instrument. During the past three years we have accumulated a large number of blood pressure charts from which a great many interesting observations could be made. These will be treated more at length in a subsequent paper. These observations were instituted as a routine procedure, because the condition of the blood pressure is the most reliable index of the patient's condition. When the normal or approximately normal blood pressure is sustained throughout the operation we are assured that the operative procedures have not been of sufficient gravity to induce shock. The blood pressure record will determine whether a sufficient amount of blood has been lost to seriously embarrass the circulation and to require the immediate use of restorative remedies, particularly normal saline solution.

The blood pressure record is the most reliable guide when considering the question of performing the operation in one or two stages. Horsley recommends the adoption of the two-stage operation in every case, without exception, and von Bergmann in cases in which the patient's general condition is below par or in which the tumor is a particularly large one. With neither of these opinions am I entirely in accord. This question should not be decided until the preliminary stages of the operation have been completed. If after the flap has been reflected and the tumor exposed the patient's condition, as indicated by the bood pressure, is entirely satisfactory there is no reason whatsoever why one should not proceed to remove the tumor without any further

delay. In the accompanying chart (Fig. 3) one sees how the normal blood pressure was maintained throughout the entire operation. It was a case in which a fibrosarcoma was found and removed almost two years ago, and the patient has remained up to the present time, as far as anyone can tell, free from recurrence. In this case it would have been folly to have postponed, until a subsequent time, the removal of the tumor. Not only is it unnecessary, therefore, in cases in which the circulation is not seriously disturbed or embarrassed to divide the operation into two stages, but it may be distinctly harmful. Codman (*Boston Medical and Surgical Journal*, July 20, 1905) found from his study of the records of cases operated upon in the Massachusetts General Hospital that an unusually large proportion of cases died from sepsis, and he believes that the two-stage operation may be partially responsible for this complication. This deduction is a reasonable one, and should be given due consideration in determining upon the advisability of operating in one or two stages.

In many cases of brain tumor the condition of hypertension has been noted; this may, however, be due to cerebral lesions other than tumors, as, for example, in cases of large intracranial hemorrhage, either epidural or subdural, and, as we have noted, in cases of cerebral abscess and tuberculous meningitis. Hypertension, however, is not invariably associated with the presence of a tumor. If the tumor is a small one, or if it is of slow growth, infiltrating and destroying the brain tissue as it increases in size, the intracranial tension will not be increased and there will be no corresponding rise in blood pressure. That the intracranial tension may be relieved by a decompressive operation has been demonstrated by the fall of blood pressure which follows this procedure. This phenomenon is noted even if no incisions have been made in the dura, or if made, have been immediately closed with sutures.

Of further interest have been the observations which were made upon the blood pressure in connection with certain procedures other than the removal of tumors. At one time it seemed to me that the circulatory disturbances, particularly the rapid increase in the rate of pulse, was the result of the sudden relief of intracranial tension following the removal of a tumor or some similar procedure. This phenomenon is more conspicuous in operations upon the cerebellum and is often associated with a fall in blood pressure. Circulatory embarrassment, occurring as a complication of cerebellar operations, is very much more readily explained, owing to the proximity of the medulla oblongata to the field of operation. In operations upon the cerebrum, however, we have been somewhat surprised to note the negative results, in so far as concerns the blood pressure, attending the evacuation of large cysts or abscesses, or even the opening of distended ventricles. I have at hand a number of charts in which the blood pressure is seen to be unaffected by any of these procedures.

It may be of interest in this connection to call attention to the absence of any relation between the rate of the pulse and the state of the blood pressure. In a great many of our cases the rate of the pulse increased very rapidly almost immediately after the operation began. This increase in the rate of the pulse seems to be altogether out of proportion to the gravity of the operation, especially when it appears before the brain has been explored. (Fig. 4.) Whatever may be the cause of this phenomenon, there is as a rule no accompanying fall of blood pressure. It is needless to say that the rate of the pulse may have no influence upon the blood pressure, but unless the condition of the blood pressure was known in the course of the operation a good deal of anxiety might arise in the mind of the operator when the rate of pulse increases rapidly to one hundred and fifty, sixty or seventy. Yet I have never seen a case in which there was cause for alarm, unless the warning had first been given by a fall in the blood pressure. If the tachycardia is unassociated with a hypotension there is no necessity for resorting to stimulation. After the operation is concluded the pulse will gradually return to normal.

Various Methods of Exposing Tumors. It is not my purpose to describe all the methods of opening the skull for the exposure of underlying lesions, as a complete list of them may be found in surgical text-books. I will refer to but a few of them, and to those only which are employed in the important clinics of this country and Europe. Unless in the performance of a palliative operation, when the permanent removal of bone is clearly indicated, the trephine is no longer used for the purpose of exposing tumors. The advantages possessed by Wagner's osteoplastic flap are so great as to prohibit the use of an instrument such as the classical trephine, which leaves a permanent defect in the skull. As to the ways of making a Wagnerian flap, I shall refer only to a few:

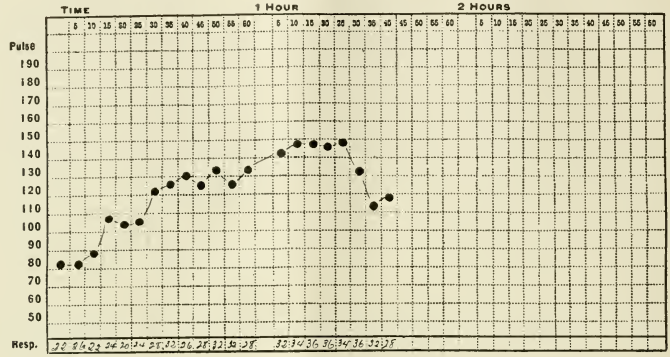
1. *Mallet and Chisel.* When Wagner first described his osteoplastic resection of the skull in 1889 he used the chisel and mallet. Since that time so many superior instruments have been introduced into the surgeon's armamentarium that the chisel and mallet have practically been discarded. As compared with any other methods this can be said of a certainty to have no advantages while possessing unquestionable disadvantages. Not only does it require very much more time to make the opening, but meanwhile a degree of traumatism is being inflicted upon the brain, which is, to say the least, undesirable.

2. *Craniotomies.* Various instruments have been devised for making sections of the skull with greater expedition than is possible either with the chisel or with a Hey or Doyen saw. The simplest of these is Dalgren's craniotome or forceps (see Fig. 5), with which a flap of any size or shape may

ANESTHESIA AND BLOOD PRESSURE RECORD.

NAME John Sampson HOSPITAL U. of P. INDEX FILE No. 624 VOL.

ANESTHESIA CHART.



Operation Craniotomy Date 5-21-'04 Operator Dr. Frazier.

Operation Started 1.40 P.M. Operation Ended 2.55

Anesthetic Ether.

Variety Squibb's Method Anesthetizer Dr. Usher.

Time to Anesthetize 15 min. Amt. to Anesthetize ℥vi Total Amt. Used ℥x

Examination of Chest (before)

BLOOD PRESSURE CHART.

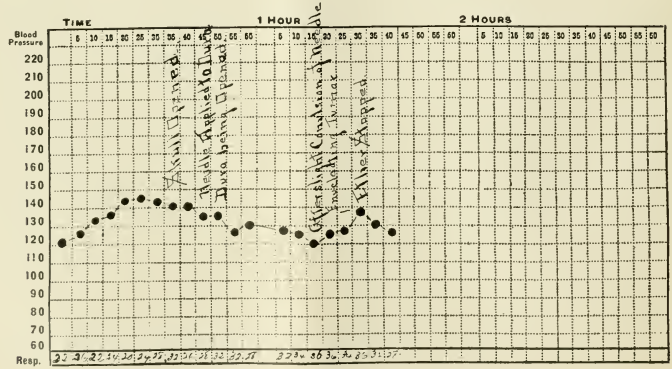
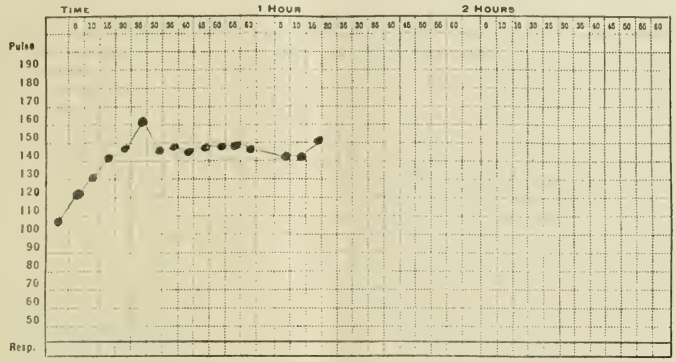


FIG. 3.—Normal blood pressure maintained throughout operation and unaffected by enucleation of tumor. Note disproportion in rate of pulse.

ANESTHESIA AND BLOOD PRESSURE RECORD.

NAME MRS CLIFF HOSPITAL INDEX FILE NO. 1207 VOL

ANESTHESIA CHART.



Operation CRANIOTOMY Date 3.15.06 Operator DR. FRAZIER

Operation Started 5.11 P.M. Operation Ended 6.23 P.M

Anesthetic ETHER

Variety SQUIBBS Method GAUZE Anesthetizer DR. ASHER

Time to Anesthetize 12 MIN. Amt. to Anesthetize 3 ii Total Amt. Used 3 iv

Examination of Chest (before) NEGATIVE

BLOOD PRESSURE CHART.

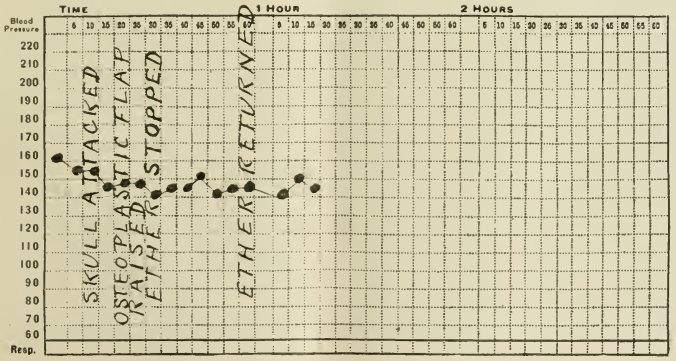


FIG. 4.—Note unusually rapid rate of pulse while the blood pressure is maintained at or about 140.

be made after an opening has been made in the skull either with a burr or trephine. When operating upon a thin skull this instrument should give entire satisfaction, and has the advantage over others in that the opening in the skull may be made of any shape that may be desired (Fig. 6). Of the other craniotomes, which resemble each other in the principles of construction and method of operation, one was devised by Codivilla (*Revue de Chirurgie*, 1900, tome ii. p. 646) and one by Stellwagen (*Annals of Surgery*, July, 1902). The method of operating these instruments is very similar: in the case of the Codivilla craniotome the saw is operated through the medium of a moderately long shaft, and in the case of the Stellwagen instrument through the medium of a handle similar to that of a trephine. Both these instruments possess many admirable features; their simplicity of construction, the ease with which they can be sterilized, manipulated and regulated to cut skulls of various thicknesses and openings of various dimensions, the possibility of operating them without the aid of a motor, make them very serviceable instruments. They are comparatively inexpensive

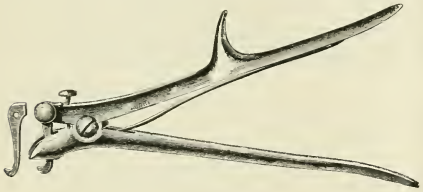


Fig. 5.—Dalgren's forceps.

and are perfectly safe in the hands of inexperienced operators. While not wishing in any way to depreciate the value of these instruments, I prefer other instruments to these, for two reasons: first, because one is obliged to make in all cases a circular opening. In many instances this is unfortunate because a portion of the area to be explored will not be exposed. Thus in exploring the occipital lobe, in order to uncover this lobe entirely, we must expose that portion of the lobe at the angle between the transverse and longitudinal sinuses, but with a circular opening this is impossible. So, too, in any case in which it is desired to explore the region bounded by the longitudinal fissure, a circular opening will "cut corners" and leave a considerable area uncovered. In a general way the lines or fissures dividing the various lobes are comparatively straight and the sides of the osteoplastic flap should run parallel to them, so that the ideal flap is a rectangular rather than a circular one. In the second place, a considerable amount of blood will be lost during the process of sawing through the bone. The greatest amount of bleeding comes from the venous channels in the diploe; with the Codivilla or Stellwagen trephine one begins to saw through the skull layer by layer from without inward until one reaches the diploe; upon reaching the inner table of the skull, one must proceed more cautiously for fear of penetrating the dura and injuring the brain. Meanwhile, hemorrhage from the diploic vessel is very free, and, of course, uncontrollable until the bone is entirely divided and the flap reflected. The spiral osteotome which we are about to describe divides the entire thickness of the skull as it proceeds; furthermore, it seems to crush and occlude the openings of the diploic sinuses, and in that way tends to arrest hemorrhage.

3. *The Gigli Saw.* Shortly after Wagner (1889) described his osteoplastic resection of the skull, Toison (1891) suggested that the bone be divided with a saw, between a

Fig. 6.—Codivilla's craniotome. (From Marion's Chirurgie de Système Nerveux.)

number of trephine openings, from within outward. The saw which he used for the purpose was a thin flexible instrument, trapezoid on cross-section. In 1897, Obalinski recommended the use of the flexible wire saw—the Gigli saw—as a substitute, and since that time the Gigli saw has been used exclusively for this operation, and various instruments have been devised by Gigli, Lauenstein and others to guide the saw from one opening to the other. A number of openings varying from three to five, according to the size of the flap, are made in the skull with a trephine or spherical burr. To protect the dura and brain from laceration these openings must not be placed too far apart; since the surface of the brain is convex, the saw if stretched across too great a space from one opening to another will of necessity come in contact with, and when in operation cut through, the dura and into the brain. If this precaution is taken the method of Toison

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and Obalinski is in many particulars an ideal one. The opening in the skull can be made of any shape or dimensions, with little traumatism and in a comparatively short time. The instruments are inexpensive, easily procurable, require no adjustment, and no especial experience or practice in their manipulation.

4. *The Circular Saw and the Spiral Osteotome.* These instruments differ from all others in this essential, in that they are operated by means of a hand or electric motor. In 1895 Doyen introduced his circular saw (see Fig. 7), which is armed with a guide inserted beneath the bone to afford protection to the underlying dura. A similar instrument has been used for a number of years by McCosh. After the incision is made in the scalp, four or five holes are

Fig. 7.—Doyen's electrical craniotome. (From Marion's Chirurgie de Système Nerveux.)

bored through the skull, as in the Toison method, with a cone-shaped burr (fraise spherique) about one-quarter of an inch in diameter. When the holes have been drilled the circular saw is substituted for the bulb and the bone intervening between the holes sawed through. As compared with any others previously mentioned the Doyen method might claim superiority solely because it is somewhat more expeditious. The presence of the guide or flange attached to the saw protects the dura, and while the same number of holes must be drilled as in the Toison method there is less difficulty in applying the circular saw, and the bone can be sectioned more rapidly.

In 1894 Cryer, then an instructor at the University of Pennsylvania, devised an instrument which he called the spiral osteotome. This was the first instrument operated by a hand or electric motor to be used in the performance of craniotomies. (See Fig. 8.) The instrument is very simple in its construction and is provided with a flange which protects the dura.

Curiously enough, very little was known of Cryer's instrument, outside of Philadelphia, until 1900, and about this time Sudeck, apparently without any knowledge of the one which Cryer and others had been using for six years devised an osteotome which is identical in every particular. Even at the present time most American surgeons familiar with the spiral osteotome refer to it as Sudeck's instrument, and this is the name invariably given the instrument in foreign literature. In my clinic at the University Hospital, in the past fifty or more craniotomies, I have used Cryer's instrument because I believe it to possess certain features which make it superior to any other. In the first place it is necessary to make but one opening in the skull, and this can be done in a few seconds with the small trephine or burr, instead of three or more as required for some of the other methods, notably Toison's and Doyen's. Secondly, a flap can be fashioned of any dimensions, with straight or curved margins

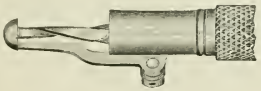


Fig. 8.—Cryer's spiral osteotome.

as the occasion demands. Thirdly, the flap can be cut more quickly than by any other method; from the time the drill is introduced until the flap is reflected but a minute or two will have elapsed. That the element of time plays no unimportant part in the outcome of operations upon the subjects of brain tumors I am fully convinced, therefore, preference should be given to the instruments which are most economical as to time.

Craniometric Lines and Craniocerebral Relations. In the concluding portion of this paper will be described a series of openings which are so arranged as to expose certain well-defined physiological areas of the brain. The shapes and size of each opening are defined according to our knowledge of certain craniocerebral relations. The variations in the shapes of the skull and in the relation of the fissures and convolutions of the brain to the skull are well known, and at first thought it might appear impracticable if not impossible to outline upon the scalp a flap which would correspond to a given area of the brain. From frequent observations on both the living subject and upon the cadaver I have been surprised to find how frequently the craniometric lines correspond to the fissures and convolutions of the brain. It will be interesting in this connection to allude to some of

the conclusions at which Froriep arrived in an investigation of the relations between the brain and the skull (*Die Lagebeziehungen zwischen Grosshirn und Schadeldach*, von Dr. August Froriep). He noted among other things that all the specimens which he examined could be divided into two groups; (1) the frontopetal (Fig. 9), or those in which the greater portion of the brain lies anterior to a vertical line drawn through the external auditory meatus, and (2) the occipitopetal (Fig. 10), or those in which the greater portion of the brain lies posterior to the external auditory meatus. In the first or frontopetal group the central fissure lies with relation to the position of the external auditory meatus farther forward and is more vertical in its course; in the second, or occipitopetal group, the central fissure lies farther back and follows a more oblique course. These two groups however, have no relation to the brachiocephalic and dolichocephalic skulls. It might at first be supposed that the frontopetal brains corresponded to the brachiocephalic skulls and the occipitopetal to the dolichocephalic skulls, but this is not the case. The position of the brain, while not independent of the form of the skull, has no relation with the proportion of the breadth to its length. It was found, however, that while there was no relation between the position of the brain and the relative length and breadth of the skull there was a relation between the length of the skull and the brain; thus the occipitopetal type of brain was found in the long skulls and the frontopetal type in the shorter skulls. The absolute measurements, as to length, are those upon which the greatest reliance should be placed in any craniometric system. Froriep also found that the position of the brain was more dependent upon the configuration of the *hinterhaupt* than upon any of the diameters of the skull. The greater the distance between the occipital protuberance and the internal auditory meatus the nearer does the form and position of the brain correspond to the occipitopetal type. It was also noticed that the nearer the brain corresponded to the extreme occipitopetal type the lower the position of the inion.

Fig. 9.—Type of frontopetal brain. (After Froriep.)

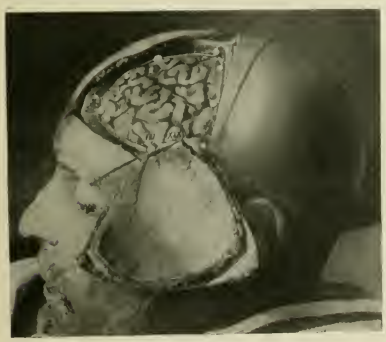
Fig. 10.—Type of occipitopetal brain. (After Froriep.)

These observations interest me, especially for two reasons: first, because he found that the absolute length of the skull could be considered a factor, which took into consideration, variations in the shape of the brain and its relations to the skull; and secondly, because he found that, based upon familiar craniometric methods, there was a variation in the position of the Sylvian or Rolandic fissures of not more than 35 to 40 mm. between the most extreme frontopetal and occipitopetal types of brain.

The calculations in the Anderson-Makin method, which we have used exclusively for determining the position of the Rolandic and parieto-occipital fissures, are based upon the length of the skull, measured from the glabella to the inion. The upper extremity of the Rolandic fissure corresponds to a point one-half to three-quarters of an inch behind the mid-point between the inion and glabella. The upper extremity of the parieto-occipital fissure corresponds to a point one-quarter of an inch behind the mid-point between the line of the Rolandic fissure and the inion. If any criticism whatever is to be made upon the Anderson-Makin method it should be upon the rules for determining the direction of the fissure. These taken into consideration the position of the external auditory meatus and the latter we have seen occupies a

variable relation to the central fissure in different types of brains. However, there is not a great deal of variation in the direction of the fissure, and if we are reasonably sure of the position of its upper extremity there will be no danger of our failing to expose it, particularly when the posterior margin of the flap is made at least three-quarters of an inch posterior to the fissure.

The illustrations of the various openings, as seen in Figs 11 to 16, were made from photographs which were taken after the operations, described in the text, were performed upon the cadaver. Before the skullcap was removed pins were introduced around the margin of the openings in order to enable one to determine positively the extent of the area



A

B

Fig. 11, A.—Prefrontal opening, showing relation to Sylvian and Rolandic fissures.

Fig. 11, B.—Area of cortex exposed in prefrontal opening, including (I) superior frontal convolution, (II) middle frontal convolution, (III) inferior frontal convolution, and (XIX) Broca's convolution.

exposed. A photograph was then taken after the skullcap was removed, and in each illustration Roman numerals have been used to indicate the important convolutions included in the opening. In almost every instance it will be seen that the outlines of the flap corresponded to the physiological area of the brain which it was intended to expose.

Tumors of the brain in their earlier stages at least are confined to one of the various physiological lobes or areas of the brain. If there be any localizing symptoms they will point to the tumor being situated in the prefrontal, the midfrontal, the postfrontal or motor, the parietal, the occipital or the parieto-temporal or visuoauditory region. These correspond to the conventional areas recognized by Dr. Mills in his discussion of the diagnosis of cerebral tumors. In the majority of cases, therefore, the surgeon is called upon to make a flap which will expose a tumor in one or the other of these regions. For these six conventional regions, therefore, we have six conventional openings. I shall describe these openings seriatim, with the aid of illustrations, and refer briefly to the history of one case for each opening.

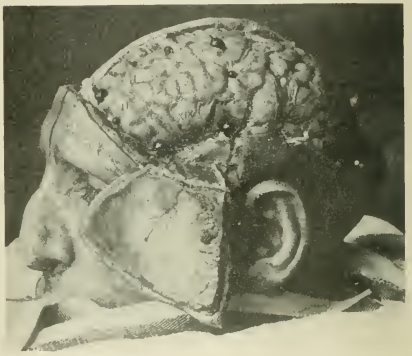
1. Prefrontal Opening. The frontal lobe, according to the usual acceptation of the anatomist, comprises on the lateral aspect of the cerebrum all that region between the cephalic extremity of the brain and the central fissure. That it is a region of high functional value is understood when it is recalled that it is subdivided into at least three great physiological areas, namely, a prefrontal or higher psychic zone, a midfrontal or intermediate psychical motor zone, a region of representation of skilled movements of speech, of writing and of the lower extremity, and probably of the head and eyes, and a fundamental motor region. When the symptoms are psychical, therefore, it will be necessary only to expose the prefrontal area, although because of the tendency of prefrontal tumors to spread backward it is advisable to have the flap large enough to expose at least a portion of the midfrontal region. The opening of the prefrontal region would have the following boundaries (see Fig. 11, A and B): Its anterior boundary should run about parallel and a little below the frontal eminence, its superior boundary one-half inch below and parallel with median line; its posterior boundary is parallel with the central or Rolandic fissure, beginning

above at a point four inches behind the upper extremity of the anterior boundary, and the base on a level with the Sylvian fissure. This opening would, measuring four inches in width and about three and one-half inches in length, expose the first, second and third frontal convolutions (see Fig. 11, A and B).

Mrs. S., aged forty eight years, referred to me by Dr. Charles K. Mills, November 9, 1903, presented symptoms of a prefrontal lesion. In this case there were no localizing phenomena other than those of a psychical nature. Patient's mental condition was rather dull and apathetic. She was very slow in answering and easily confused. Her memory was evidently impaired. In addition to these phenomena, the patient had the usual symptoms of brain tumor, headache, optic neuritis and vomiting. Under ether anæsthesia an incision was made corresponding to the one which we have described as suitable for this region, exposing the three frontal convolutions. The region was explored with absolutely negative results. The patient died ten days after the operation, and an autopsy revealed a tumor in the cerebellar pontile angle and a very marked internal hydrocephalus. The latter condition was responsible no doubt for the disturbance of function in the frontal lobes and naturally led to an error in diagnosis.

2. Midfrontal Region. The opening in a case of tumor in which at least the initial effects point to the growth being situated in the third or second frontal convolution, no matter what may be the other symptoms, should be so placed that the third frontal convolution will be found in about the middle or just below the middle of the opening. This flap (see Fig. 12, A and B) differs from that for prefrontal tumors in that the superior margin is about an inch or inch and a half from the median line and the base or inferior margin is below the line of the Sylvian fissure, over the anterior limits of the temporal lobe. The anterior and posterior margins differ in no respects from those in the flap for the prefrontal region except in so far that they terminate an inch or an inch and a half from the median line and may each be made a little more posteriorly to the prefrontal opening. In addition to the agraphia and aphasia there were in the following cases symptoms pointing to invasion of a portion of the motor cortex. In this case it was necessary to modify the shape of the regular midfrontal flap so that it exposed a portion of the motor zone as well.

A



B

Fig. 12, A.—Midfrontal opening extending below Sylvian fissure and not including first frontal convolution.

Fig. 12, B.—Area exposed by midfrontal opening, including (II) middle frontal convolution, (III) inferior frontal convolution, and (XIX) Broca's convolution.

J. S., aged twenty-eight years, was admitted to the University Hospital, May 20, 1904. He was sent to the hospital by Dr. J. W. McConnell, with the following history: Four years ago he had his first convulsion; a year later a second; six

months later a third. From that time on the convulsions appeared with increasing frequency, but with less severity. At first they were associated with loss of consciousness, but more recently consciousness has been preserved. Dr. McConnell described the attacks which he saw as follows: There was fixity of gaze, blubbering movements of the lips, increased secretion of saliva, twitching of corner of the mouth and twisting of head to the right, with clonic spasm of the entire right side of the face. There was no loss of consciousness. When told to, the patient moved his hands during the spasm. The right pupil was dilated during the attack, the eyes were in the median line and the spasm involved the orbicularis palpebrarum. After the attack his speech was very much impaired, in fact for a few moments he was unable to speak at all. When speech returned it was as that of an intoxicated person. There was evidence of involvement of the right facial nerve. It was further noted that though the patient was an educated man, his writing was absolutely unintelligible. He neither could spell the words nor make the characters. A craniotomy was performed, and a tumor occupying portions of the superior and middle frontal convolutions, possibly the upper extremity of the third frontal convolution, was exposed. The tumor was removed and upon examination proved to be a sarcoma. The patient made an excellent operative recovery, and has up to the present writing remained free from recurrence.

3. Parietal Opening. The loss or impairment of stereognostic conception and impairment of muscular and cutaneous sensibility suggest a lesion of the parietal lobe. When there are no other localizing symptoms the opening in the skull should be so made as to expose the region between the motor area and the occipital lobe, the anterior margin running parallel with and just posterior to the Rolandic fissure, the posterior margin beginning at the parieto-occipital fissure and extending downward along a line nearly parallel with the anterior margin (see Fig. 13, A and B). I have never been called upon to operate for the removal of a tumor confined to the parietal lobe, but the following case—a gunshot wound—will serve as an example of an instance in which it was necessary to make a parietal opening:

A

B

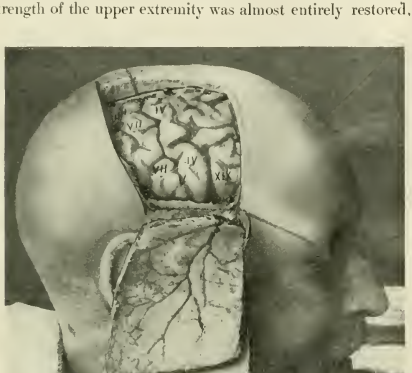
Fig. 13, A.—Parietal opening showing relation to Rolandic and Sylvian fissures. Posterior margin corresponds to line of parieto-occipital fissure. Note in Fig. 13 B (IX) how accurately this fissure was localized by craniometric method.

Fig. 13, B.—Area exposed in parietal opening, as indicated by black pins, including (VII) postcentral convolution, (VIII) intraparietal fissure, (XX) angular gyrus. Compare Fig. 13 B with 13 A and note how accurately the Rolandic fissure V and the parieto-occipital fissure IX had been localized.

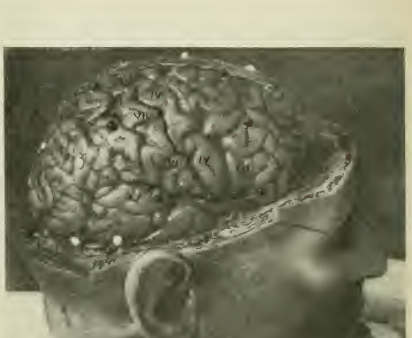
The patient, C. J., aged fourteen years, sustained an injury from the discharge of a revolver; the bullet entered the left temple and passed upward and backward, lodging, as it was supposed from a skiagraphic study and from the symptoms, in the right parietal lobe. There was very evident impairment of stereognostic conception in the left hand. In addition to this significant symptom there had been some convulsions involving the entire right side of the face and the right upper and lower limb. The convulsions ceased, however, and there remained paralysis of both the upper and lower limb. Sensation for touch and pain in the lower limb was normal, but, as stated above, stereognostic conception was impaired in the

left hand. The motor symptoms were attributed to the injury which the motor tracts had sustained as the bullet passed through to the parietal lobe. Furthermore, a very accurate calculation, based upon the skiagraphic study, localized the bullet in the parietal lobe about an inch from the cortex. After carefully considering the symptoms and the skiagraphic evidence the parietal lobe was exposed and an attempt made to find the bullet with an exploratory needle. In this, however, we were not successful and inasmuch as the bullet was believed to be at least an inch from the surface, it did not seem justifiable to continue the search by making an exploratory incision. When the patient was discharged from the hospital the strength of the upper extremity was almost entirely restored, but there remained some weakness in the peroneal and tibial group of muscles in the lower extremity.

The cranial nerves were not affected. Tactile sensation was normal on both sides of the face. The grasp of the left hand was feeble, and there was slight diminution of sensation for both touch and pain in entire left upper limb. Stereognostic perception in the left hand was entirely lost. The patient complained of persistent and severe headache and had occasional convulsions, which began in the abdominal muscles and involved the left side of the face, and left upper and lower limbs. Under such circumstances it was necessary, of course, to reflect a flap which would include both the motor and parietal regions. The posterior margin of such a flap should correspond to an extension of the line of the parieto-occipital fissure, but the anterior margin need not be made quite so



A



B

Fig. 14, A.—Standard motor opening, showing accuracy with which flap had been marked out with relation to V or Rolandic fissure.

Fig. 14, B.—Area exposed in motor opening, as indicated by *black* pins, includes (IV) precentral convolution, (V) Rolandic fissure, (VII) postcentral convolution, and (XIX) Broca's convolution. Note how accurately the base of the flap corresponds with VI, the Sylvian fissure. Both the Rolandic and Sylvian correspond exactly with the lines which were marked upon the scalp before the flap was reflected.

In every instance, providing the lesion is of recent formation or is of small dimension, the localizing symptoms will point to functional disturbances in but one physiological area. In cases of long duration the lesion may grow beyond the limits of one physiological area and involve that adjacent to it. Thus, for example, a tumor may begin in the parietal lobe and extend to the occipital or motor region. Such was the history of the following case:

M. McJ., aged thirty-nine years, under the care of Dr. William G. Spiller, was admitted to the University Hospital October 11, 1904. There were no abnormal ocular phenomena.

far in advance of the Rolandic fissure as would be necessary when the tumor was believed to have originated and to have remained localized in the motor area. Under such circumstances the anterior margin of the flap is usually made two to two and a half inches in front of the Rolandic fissure. An opening of this description was made in the case just alluded to and a large infiltrating gumma found and removed. The operation was unattended with any difficulties and the convalescence was uncomplicated.

Motor Opening. In a paper recently published ("The Motor Area of the Cerebrum, its Position and Subdivisions, with Some Discussion of the Surgery of this Area," by Charles K. Mills, M.D., and Charles H. Frazier, M.D., University

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of Pennsylvania Medical Bulletin, vol. xviii.) conjointly with Dr. Mills, I wrote somewhat at length upon the position of the motor area and upon the shape of the motor flap. For the exposure of this area we had adopted a standard motor opening in connection with some observations which were being made upon the position of the motor cortex with relation to the central fissure. The results of our observations upon the human subject, taken in connection with the experiments of Grunbaum and Sherrington upon the anthropoids, led us to believe that the motor zone in man at least is entirely or almost entirely in front of the fissure of Rolando. For this reason the motor flap is so mapped out that at least two-thirds or three-fourths of the opening lie in front and not more than one-third or one-fourth posterior to the Rolandic fissure. The lines corresponding to the central and Sylvian fissures are marked upon the scalp; the posterior margin of the opening runs parallel with and about three-quarters of an inch behind the central fissure; the superior margin should not extend nearer than one-half an inch to the median line and the base of the flap crosses the Sylvian fissure (see Fig. 14, A and B). A forward central extension of the opening should be outlined on the scalp to cover what is believed to be the most anterior portion of the area for the eyes and head. If the flap measures three and a half to four inches in width it will be wide enough to expose this area. It may be necessary in some cases to rongeur away the bone at the upper margin of the opening if the lesion is found to be near the longitudinal fissure. I have been called upon to expose the motor area more frequently than other areas, and have found the opening which we had adopted most satisfactory.

G. K., aged fifty-two years, was admitted to the University Hospital under the care of Dr. William G. Spiller, May 1, 1903. The significant features of the history were as follows: Headache of several years' duration, becoming more and more constant and more and more severe; weakness in the right upper extremity; convulsions involving the right side of the face and right arm, and motor aphasia. Dr. de Schweinitz reported that this was only a suggestion of a choked disk. Upon reflection of a motor flap an area was exposed to view which was evidently pathological and proved to be a tumor. The tumor was situated near the anterior margin of the opening, so that if the latter had been a little smaller the tumor would not have been exposed. The patient's condition at this time was entirely satisfactory, so that there was no necessity for postponing the removal of the tumor until a subsequent time. The extirpation of the growth was proceded with and attended with no technical difficulties. The

A

B

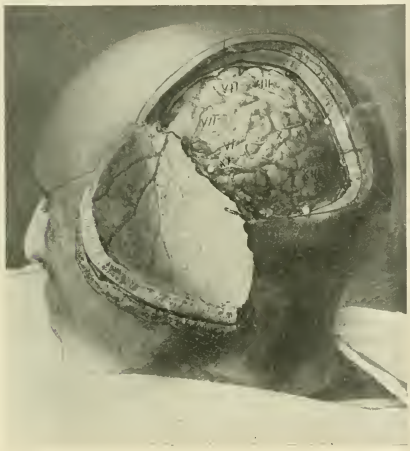
Fig. 15, A.—Occipital opening.

Fig. 15, B.—Area exposed in occipital opening as indicated by *white* pins, includes (XII) superior occipital, (XIII) midoccipital, and (XIV) inferior occipital convolutions, also a portion of (XI) first temporal convolution. This opening is not intended to include (XX) the angular gyrus, and the illustration shows it just on the outskirts.

patient recovered from the immediate effects of the operation; on the fifth day it was observed that his aphasia was very much better, both as to the size of his vocabulary and as to the rapidity with which he could give expression to his thoughts. The headache of which he had complained so bitterly was almost entirely relieved. Subsequently the tumor, which was found to be a sarcoma, recurred, and the patient eventually died.

The Occipital Opening. This opening is used in cases in which the predominant symptom is hemianopsia. To expose the occipital lobe the flap should extend posteriorly to the line of the lateral sinus, anteriorly to the parieto-occipital

The patient, M. B., aged seventeen years, was transferred to me from the service of Dr. Mills, October 9, 1904, with the history of having been struck on the back of the head nine months before. He was not unconscious at the time he fell. About an hour later he became dazed, walking around aimlessly, and remaining in this state for about half an hour. On January 28, 1904, he was seized with shortness of breath, succeeded by tingling in the ears, and fell to the ground. It was said that during the convulsion his eyes were turned from side to side and that the whole body, with the exception of the hands and wrists, fell into a state of spasm lasting from five to seven minutes, with frothing from the mouth. Since



A

B

Fig. 16, A.—Parieto-occipital opening.

Fig. 16, B.—Area exposed in parieto-occipital opening: V, Sylvian fissure; VII, precentral convolution; VIII, intraparietal fissure; IX, parieto-occipital fissure; XII, superior occipital convolution; XIII, midoccipital convolution; XX, Broca's convolution. The anterior margin of the flap, which was mapped out upon the scalp so as to run parallel with and just behind the Rolandic fissure, proved to be almost on a line with the fissure. Likewise the position of the parieto-occipital proved to have been very accurately localized before the flap was reflected.

fissure and above to within half an inch of the median line (see Fig. 15, A and B). The parieto-occipital fissure is situated approximately one-quarter of an inch posterior to a point midway between the inion and the line of the Rolandic fissure. The reflection of this osteoplastic flap is attended with some risk because of the proximity of the posterior and superior boundaries to the transverse and longitudinal sinuses respectively. It is most important that the entire occipital lobe should be exposed, and yet one must be exceedingly careful in reflecting the dural flap not to injure either of these large sinuses. The following is a case in which the operation for the exposure of the occipital lobe was performed:

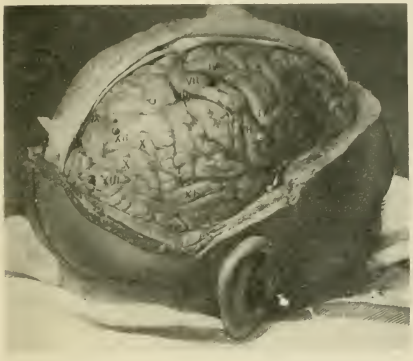
that time he has had five attacks of this character, the latter one having been preceded by violent occipital headache and vomiting. He has marked optic neuritis, complains of intense headache and occasionally vomits. There is no hemiasynergia of either side. The patellar reflexes are normal. Hearing is not markedly affected. There is no paralysis of either facial nerve. Sensations for pain and touch are undisturbed. The movements of the extraocular muscles are normal, but there is nystagmus in looking either to the right or left. Stereognostic perception is normal in both hands. There is no disturbance of the reflexes and no muscular atrophy in any extremity. Inasmuch as the symptoms pointed

entirely to the occipital lobe, a craniotomy was performed in this region. It was noted, upon reflection of the flap, that there was but slight pulsation and great tension, and when the dural flap was turned back the brain at once bulged through the opening. There was no evidence of a neoplasm on the cortex. The brain had protruded so through the opening that it was necessary in order to cover the defect to use a flap from the pericranium and also to remove the bone from the osteoplastic flap. The patient enjoyed considerable relief in so far as the headache, vomiting and dimness of vision were concerned, but the hernia which developed after the operation continued to increase in size and the optic neuritis recurred.

There are certain cases in which, in addition to hemianopsia, there are symptoms suggesting some lesion in the neighborhood of the visuoauditory centres. Under such circumstances the anterior margin of the flap should be three-quarters to one inch in front of the line of the parieto-occipital fissure, the posterior and superior margins corresponding to those used for the simple occipital opening.

In other cases there may be symptoms pointing to a lesion not only in the parietal region but also in the region of the visuoauditory centres. In the one case we are called upon to make an occipitoparietal opening or an occipital opening extending about an inch in front of the parieto-occipital

A



B

FIG. 17, A.—Parietotemporal opening.
FIG. 17, B.—Area exposed in parietotemporal opening, including the temporal as well as the parietal convolutions.

He was re-admitted to the hospital December 21, 1904. The original flap was reflected, an exploratory canula introduced and a large cyst discovered, extending to within one-half inch of the brain cortex. Upon evacuation of the cyst the brain collapsed and the dural and musculocutaneous flaps were replaced without any difficulty. With the exception of this disturbance of vision, which was not entirely relieved by the second operation, the patient's health is excellent.

In February, 1906, a letter was received, stating that he had had no "bad spells." The hernia which had developed at the site of the operation has not increased in size for the past year, but has remained about stationary.

fissure; in the other, a parieto-occipital opening (see Fig. 16, A and B) that is a parietal opening extending three-quarters to one inch behind the occipitoparietal fissure. Some cases may point to a lesion of the angular gyrus alone, and under these circumstances the line of the occipitoparietal fissure should correspond with the middle of the flap.

Finally, there may be instances in which the symptoms refer to a lesion not only in the parietal but in the temporal region, in which case the flap must be so placed that its base is sufficiently below the line of the Sylvian fissure to expose the temporal convolutions. (See Fig. 17, A and B.)

A STUDY OF THE BLOOD IN LEAD POISONING, WITH A DESCRIPTION OF THE BONE-MARROW OF ONE FATAL CASE.

By Williams B. Cadwalader, M.D.

(From the Ayer Clinical Laboratory of the Pennsylvania Hospital, Philadelphia.)

Although much time has been devoted to the study of the changes brought about in the erythrocytes by lead intoxication, very little attention has been paid to the proportions and varieties of both the red and white cells, which, when considered collectively, present a very definite and characteristic picture.

The most important point in regard to the red corpuscles is the comparatively slight reduction in their number, the basophilic granulations and the presence of nucleated red cells, megaloblasts as well as normoblasts, may be found in the general circulation. The appearance of nucleated red cells in the circulating blood has generally been considered as the natural sequence of a severe anæmia, and usually looked upon as a reparative process. In a previous communication[1] an attempt was made to show that there was a definite relation between the number of nucleated red cells and the number of non-nucleated red cells containing basophilic granules, and that the number of erythroblasts was not proportionate to the anæmia present. It was then suggested that this blood picture was due to some toxic effect of lead upon the hæmopoietic organs.

The present paper embodies a series of observations on the number and percentages of the white cells as well as the red blood corpuscles.

Total and differential blood counts were made upon thirty-seven cases of lead poisoning, all of which presented the well-known symptoms, *i. e.*, colic, constipation, blue line on gums, tremors, etc., and a clear history of having worked in lead for periods of from a few weeks to many months.

The hæmoglobin and the erythrocytes were reduced to about one-fourth of the normal in most cases, giving an average of about 65 per cent. hæmoglobin and 3,850,000 red cells per 1 cm. In every instance there was a marked increase in the number of granular red blood corpuscles. Macrocytes and microcytes were occasionally met with, but poikilocytosis was, as a rule, not marked. One or more normoblasts were found in all but four cases, and megaloblasts in two instances, while in one case one hundred and thirty normoblasts and thirteen megaloblasts were found while counting five hundred white cells, notwithstanding the fact that the total number of erythrocytes was scarcely one-fourth less than the normal.

[1] Bulletin of the Ayer Clinical Laboratory of the Pennsylvania Hospital, January, 1905, No. 2.

No. of case.	Per cent. of hæmoglobin.	Red cells per 1 cmm.	Per cent. of basophilic granular R. B.C.	Poikilocytosis.	Leukocytes per 1 cmm.	Polymorphonuclear.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Basophiles.	Myelocytes.	Normoblasts in counting 500 white cells.	Megaloblasts in counting 500 white cells.
						%							
1	67	4,852,000	—	—	9450	73.6	15.8	9.0	1.0	0.6	0	2	0
2	80	4,025,000	—	+	8150	57.2	32.0	8.4	2.0	0.4	0	5	0
3	88	4,788,000	—	—	10000	71.4	17.8	9.2	1.2	0.4	0	4	0
4	76	4,400,000	—	+	7500	64.0	26.4	8.4	0.6	0.6	0	2	0
5	52	2,828,000	18.0	++	12350	77.2	11.6	10.8	0.4	0.0	0	4	0
6	98	4,680,000	—	+	7400	66.0	16.0	15.4	2.0	0.6	0	2	0
7	70	2,620,000	5.0	++	5800	66.8	21.4	7.4	4.0	0.4	0	2	0
8	85	4,424,000	6.3	+	11750	79.0	16.0	4.4	0.4	0.2	0	2	0
9	78	4,472,000	13.0	+	7500	77.2	6.0	16.8	0.0	0.0	0	3	0
10	62	4,672,000	9.5	+	7200	77.8	17.6	4.2	1.4	0.0	0	1	0
11	76	3,800,000	14.0	+	10000	76.6	4.6	17.6	1.2	0.0	0	130	13
12	75	3,860,000	9.2	+	12200	71.8	6.8	20.0	1.4	0.0	0	75	9
13	77	3,850,000	18.0	+	7300	61.6	23.2	15.2	3.6	0.0	0	10	0
14	72	4,056,000	—	+	6200	79.0	11.6	8.8	0.2	0.2	0	2	0
15	68	3,356,000	14.4	+	8500	78.8	6.4	14.0	0.6	0.2	0	25	4
16	65	2,976,000	7.8	+	5800	60.0	28.4	10.6	1.0	0.0	0	2	0
17	65	4,264,000	3.4	+	6500	76.0	20.0	3.7	0.3	0.0	0	0	0
18	60	3,400,000	2.8	+	9200	58.0	34.0	6.4	0.8	0.8	0	3	0
19	75	4,732,000	0.8	+	9000	70.4	21.2	9.2	0.0	0.0	0	0	0
20	65	3,256,000	9.6	+	6800	69.5	23.0	6.4	0.8	0.2	0	1	0
21	75	4,116,000	5.6	+	8600	75.2	5.2	18.8	0.2	0.2	0	1	0
22	70	4,300,000	5.3	+	10000	53.0	31.6	15.2	0.2	0.0	0	1	0
23	68	4,040,000	3.7	+	6600	77.6	11.0	9.8	0.8	0.8	0	0	0
24	55	3,404,000	4.0	+	6000	70.0	15.0	13.4	1.0	0.4	0	1	0
25	78	4,560,000	6.5	+	7800	76.6	13.4	8.8	1.0	0.2	0	0	0
26	70	3,800,000	6.3	+	9700	66.6	22.0	10.6	0.2	0.6	0	1	0
27	79	4,808,000	1.3	—	10100	66.4	29.6	4.7	1.3	0.0	0	1	0
28	75	3,496,000	9.0	+	7600	72.8	18.0	6.4	2.6	0.2	0	43	0
29	69	3,446,000	8.0	+	7800	73.0	23.4	2.4	1.0	0.2	0	26	0
30	71	3,498,000	5.0	+	7500	61.2	36.2	2.2	0.2	0.2	0	8	0
31	73	3,560,000	3.0	+	5600	63.8	7.0	27.2	1.6	0.4	0	9	0
32	67	3,576,000	1.5	+	5500	58.0	20.0	27.2	3.4	1.4	0	6	0
33	65	3,572,000	6.6	+	5400	70.2	24.2	4.6	0.8	0.2	0	4	0
34	72	3,640,000	8.2	+	6000	79.0	11.6	8.8	0.2	0.2	0	10	0
35	74	3,744,000	5.2	+	4700	59.2	23.8	17.0	0.2	2.2	0	3	0
36	70	3,760,000	4.1	+	5400	64.2	14.2	21.0	0.2	0.4	0	5	0
37	67	3,988,000	5.0	+	8700	69.0	18.0	12.2	0.6	0.2	0	3	0

After convalescence was established the nucleated red cells disappeared from the circulating blood before the granular erythrocytes, which slowly decreased in numbers. The total number of red cells very gradually approached the normal. In one case, the blood of which was studied during some length of time, the red cells had only increased forty thousand in four weeks after all symptoms had disappeared, while granular erythrocytes were still easily demonstrated. It would seem as if the intense pallor so characteristic of this condition, could not be wholly dependent upon so slight an anæmia, and may possibly be caused in part by a contraction of the peripheral capillaries, as has been suggested.

The leukocytes showed no morphological changes. The greatest number per 1 cm. was found to be 12,550, while

the lowest was 4700, giving an average of 7568. Cabot[1] found in fifteen cases a moderate leukocytosis, his maximum count was 24,400 and the minimum 4250, with an average of 12,922.

Boston[2] studied sixteen cases with the same results. He gives his highest count as 25,500, the lowest as 4000, with an average of 12,600 per 1 cm.

The results found in this study show a marked difference from those of Cabot and Boston. In the great majority of cases the number of leukocytes either above or below the normal was very slight. In most instances there was an increase in the percentages of the large mononuclear lymphocytes, the average being fourteen per cent., accompanied with a slight diminution in the percentages of either the polymorphonuclear cells or the small lymphocytes.

This fact has also been noted by Simon,[3] who found a somewhat greater difference in the percentages of these cells than was observed in this series. The small mononuclear lymphocytes averaged 17.8 per cent., and in general it may be said that neither in the numbers nor in their relative percentages of the white cells does the blood of individuals suffering from lead poisoning show any marked deviation from the normal.

Boston found a small number of myelocytes in all of his sixteen cases, but I have not been able to find a single one in any case studied.

Gilbert[4] speaks of eosinophilia as being characteristic of lead poisoning, but in none of these cases could this be demonstrated.

A typical case of lead poisoning was admitted to the wards of the Pennsylvania Hospital suffering from colic, constipation, etc. He gradually became worse and finally died with cerebral symptoms on the seventh day after admission. Unfortunately, no complete study of the blood was made before death. The presence of red cells showing basophilic granulations in great numbers was, however, noted. The autopsy was performed by Dr. Longcope.

Anatomical Diagnosis, No. 650. Chronic diffuse nephritis, cloudy swelling and congestion of organs.

Special interest was attached to a study of the bone-marrow. In the ribs it was deep purple in color. In the central portion of the femur it was yellow and fatty, but toward the head became deep blackish purple in color.

Sections were made from marrow of the femur and stained with hæmatoxylin and eosin. There is a marked hyperplasia of the marrow cells, giving almost a solid marrow in some places. About the margins through most sections there are a few fat cells between the hyperplastic patches, and usually a good deal of fat toward the centre. The most striking feature is the great number of nucleated red blood corpuscles. They form rather large, compact, irregular areas readily picked out under the low power of the microscope, for the nuclei stain very deeply and give these areas a blackish color. Toward the centre of these erythroblastic areas the cells are very large and closely packed together, and the nuclei frequently show irregular nuclear figures. About the periphery the cells are more scattered, and here most of them are small and appear to be normoblasts. Frequently the margin of one area fuses with the margin of another and many of them lie along bloodvessels. Between these areas the spaces are filled with white cells, principally granular myelocytes, transitional forms, a few polymorphonuclear cells, a moderate number of large and small lymphocytes and a few eosinophiles. But the hyperplasia of the leukoblastic tissue consists principally of an increase in the number of granular myelocytes, some of which show karyokinetic figures. There are a few large phagocytic giant cells.

As there had not been a complete examination of the blood made before death, we do not know what degree of anæmia existed, but it is probable that the blood picture in this case would not have been very different from many others of this series.

It is evident that lead may cause an anæmia in one of the following ways: First, by an excessive destruction of red cells in the circulation; second, by an insufficient or defective hemogenesis, or third, by a combination of these factors. The blood picture gives evidence of each of these factors as playing a part.

Ehrlich and Lazarus recognize the probability that all anæmia producing influences stimulate the marrow to hyperplasia.

Bunting,[1] while studying the effects of artificial myelotoxic sera on the bone-marrow of rabbits, found there was a definite arrangement of both the leukocytic and erythroblastic cells of the marrow in nests and groups, and of the erythrogenetic groups, the megaloblasts formed the proliferating centre. Peripherally to the megaloblasts nucleated cells of a smaller type with vesicular nuclei are seen, outside of this zone normoblasts with pyknotic nuclei and at the extreme periphery mature red cells. He thinks that the normal development of the red corpuscle is as follows: A division of the megaloblastic cell produces either its like or a smaller cell, which is often spoken of as an "intermediate" form of nucleated red corpuscle. By reproduction of these the normoblast results, while by a still further change and the absorption of a pyknotic nucleus the

[1] The Clinical Examination of the Blood, 1904.

[2] The Proceedings of the Philadelphia County Medical Society, 1902, p 246.

[3] International Clinics, 1902, vol. i. p. 69.

[4] Bulletin de l'Acad. Roy. de Med. de Belgique, 1903, p. 78.

[1] Johns Hopkins Bulletin, June, 1905.

mature non-nucleated cell develops. As a result of this grouping of the erythrogenetic cells the older and more mature red cells are constantly pushed toward the periphery by the division of the cells in the centre, and thus the non-nucleated red cell comes to lie farthest away and nearest the capillaries, and in this way after stimulation the bone-marrow is able to respond with mature red corpuscles.

Bunting further contrasts the two types of experimental anæmias produced in animals on the one hand by bleeding and on the other by injections of ricin. With the first method a marked reduction in the number of red blood cells takes place, with the presence of but few normoblasts in the circulating blood, which appear immediately after the bloodletting. With ricin poisoning there is some destruction of the red blood cells in the circulation, for hæmaglobinuria follows and one finds deposits of pigment in the organs; but in contrast to the anæmia following hemorrhage great numbers of normoblasts and megaloblasts appear in the circulation, and are to be found for some time after the injection of the poison. Bunting considers that after hemorrhage there is hyperplasia of erythrogenetic centres of the bone-marrow, but since the marrow itself is not injured the production of red cells follows its normal course. Except for a few normoblasts only adult cells reach the circulation. Ricin destroys the cells of the circulation to a certain extent, but likewise attacks the marrow cells so that the anæmia is in part due to defective hæmatogenesis. Owing to the effect of the poison upon the marrow cells, both normoblasts and megaloblasts are carried into the circulation, for adult cells cannot be formed with sufficient rapidity.

In no other secondary anæmia does there seem to be such a great effort to repair so slight an anæmia as is shown in most cases of lead poisoning. It is possible that lead may have a destructive influence upon the red cells of the circulation, but it seems most probable that its greatest influence is exerted upon the cells of the bone-marrow. Following the slight injury to the marrow cells there is overproduction, and in order to supply the necessary number of red blood cells for the circulation many immature cells, represented by normoblasts and megaloblasts, are thrown out into the circulation.

The bone-marrow picture seems to substantiate this idea. In one case studied the hyperplasia of the red blood forming cells was very striking and the erythrogenetic centres, as described by Bunting, could be made out without difficulty. In fact the changes in the marrow resembled very closely those described by Bunting in his case of ricin poisoning in animals.

BOOK REVIEWS.

THE PRACTICE OF MEDICINE. By JAMES TYSON, Professor of the Theory and Practice of Medicine in the University of Pennsylvania. Fourth edition. Pp. 1302. Philadelphia: P. Blakiston's Son & Co., 1906.

Tyson's *Practice of Medicine* is so well known that an exhaustive review of the fourth edition, which has just come from the press, is hardly called for. This work has always been essentially a conservative guide for the young practitioner or the student in medicine, with careful and exhaustive instruction, especially as to diagnosis, and giving not too small a space to the various methods of treatment. At the same time, the author has ever been on his guard against accepting the newer views and theories as they appear, but rather waiting until investigation and experience has justified the perhaps too eager claims which at first frequently accompany their introduction.

The section on Animal Parasites has been revised and in most part rewritten by Professor Allen J. Smith, a recognized authority on this subject, which has become so much larger, and attracted so much more attention as the increase in our knowledge and its practical application has gone on. Over one hundred illustrations now accompany this section alone.

The section on Diseases of the Nervous System, which was revised by Professor William G. Spiller first for the second edition, and which has attracted so much praise, has been kept well abreast of the times by the same authority.

The sections on Diseases of the Urinary Organs and on the Infectious Diseases, to mention only two, have been brought up to date by the author.

There is little reference to the increasing knowledge which the physiological chemists are now bringing to the notice of the medical profession along the lines of metabolism, and we rather expected that some mention would be made of some of the diagnostic helps which they show. Possibly, also, there should be a reference under the intoxications to chronic acetanilid poisoning, owing to the added attention which has been called in the past year to this condition, caused by the over-free sale of the patent headache tablets.

H. K. H.

A TEXT-BOOK OF DISEASES OF WOMEN. By B. C. HIRST, M.D. Second edition. Philadelphia and London: W. B. Saunders & Co., 1906.

The second edition of this work, following as it does so quickly after the publication of the first edition, shows how well this book has been received by the profession It consists of 741 pages, and is profusely illustrated. The author has drawn freely from his rich clinical material, a large number of the illustrations being from his own cases. The illustrations are as a rule excellent; this is particularly true of the illustrations of cases and the diagnostic drawings. Many of the histological illustrations are from photo-

B. J. C. D.

micrographs, and some of these are not as clear as could be wished.

The book is divided into twelve parts. Part I. takes up gynecological examination and local treatment. This latter is dealt with at some length, and will be of great practical value to the general practitioner.

Parts II. and III. deal with the anomalies of the genital tract ,diseases and injuries to the vulva and coccygodynia. Parts IV. and V. treat of the diseases and injuries of the vagina. In lacerations of the pelvic floor the author recommends a slightly modified Emmet operation, and uses silkworm-gut sutures throughout. In operating for cystocele the author describes his own operation in detail. This consists of two lateral denudations and the bringing together of certain muscular structures which the author finds in the anterior vaginal wall.

Part VI. treats of the displacements of the uterus. In selecting operation for retrodisplacements the Alexander operation is recommended for those cases in which it is not necessary to open the abdomen; it is available in about one-sixth of all the cases. In those cases in which it is thought best to open the abdomen the following operations are recommended in the order named: Suspension of the uterus; the Ferguson-Gilliam operation, and the Richelot-Dorér operation.

Parts VII. and VIII. deal with the diseases of the endometrium; disorders of menstruation; sterility; disease of the Fallopian tubes, and extrauterine pregnancy.

Part IX. treats of the diseases of the ovary. Under the subject of Papilloma the author has found fifty per cent. of these to be adenocarcinoma. This proportion is much higher than is usually found.

Parts X. and XI. deal with the diseases of the pelvic connective tissue, of the peritoneum, and diseases of the urinary tract.

Part XII. describes the technique of gynecological surgery as performed by the author. Taken as a whole the book is an unusually practicable one; it is well printed, and there are few typographical mistakes. Literary references will be found at the foot of each page. C. C. N.

Modern Materia Medica and Therapeutics. By A. A. Stevens, A.M., M.D., Lecturer on Physical Diagnosis in the University of Pennsylvania; Physician to the Episcopal Hospital and to St. Agnes Hospital; Fellow of the College of Physicians of Philadelphia, etc. Fourth edition, thoroughly revised in conformity with the Eighth Revision (1905) of the United States Pharmacopœia. Octavo, 670 pages. Philadelphia and London: W. B. Saunders & Co., 1905.

The call for another edition of this excellent treatise so soon after the last edition speaks well for the reception of the present volume. The changes in nomenclature, changes in strengths of different preparations and the addition of new compounds are based on the recently published Eighth Decennial Revision of the United States Pharmacopœia. New articles have been introduced dealing with scopolamine, ethyl chloride, theocin, veronal and radium, and the section on radiotherapy has been enlarged to meet the advances in this subject.

The drugs are considered by classes instead of in alphabetical order, a plan which we feel has many advantages. The subject-matter is brief and to the point, but clearness of expression has in no way been sacrificed. The section on General Anæsthesia, however, might have been improved by a more detailed description of methods and dangers. Especially interesting is the chapter on antitoxins and toxins, in which, in a few pages, the author has given an excellent résumé of the theories and present status of this most complicated question. Another chapter on remedial measures other than drugs, dealing with electricity, massage, heat, cold, hydrotherapy, actinotheraphy, etc., should prove very valuable to anyone in the practice of medicine.

The last 165 pages are devoted to therapeutics applied to special diseases. The treatise is unusually complete and is well arranged for reference or exhaustive study. The printing is clear and distinct, and, in a word, we cannot recommend the book too highly to the profession. F. H. K.

A Text-book on the Practice of Gynecology. For Practitioners and Students. By William Easterly Ashton, M.D. Second edition. Philadelphia and London: W. B. Saunders & Co., 1906. Octavo, 780 pages.

Dr. Ashton states in his preface that he has undertaken a work which aims to take nothing for granted in describing gynecological diseases, and which not only states what should be done in every case, but also gives directions and illustrations so explicit that they may be intelligently and easily followed. In this he has succeeded most admirably. As a consequence the volume as a whole is less readable than it would be if details were not so frequently repeated. The directions given for taking smears and sections of tissue for microscopic examination are very complete, and as good as any to be found.

Nothing is said of any form of operative treatment which is not in general use. The author details only those operations and plans of treatment which he himself uses. For this reason, as an exposition of gynecology, the book is not complete.

Too much importance is given to the subject of endometritis, and the classification adopted is far from convincing. The directions given for the selection and the application of pessaries are insufficient.

The operative technique described and recommended is not always the most generally approved and modern.

The discussion of certain subjects is lacking from a scientific standpoint. This is very noticeable in the section on Ovarian Cysts. Nothing is said of the adenomyomata. The illustrations are all semidiagrammatic: they serve their purpose very well, but from an artistic standpoint and for accuracy and proportion they are poor. As a whole, the volume answers its purpose very well. It is one of the best of books for the general practitioner, who will find valuable guidance in the diagnosis and treatment of gynecological diseases, and the book contains many details which are well worth the attention of any experienced gynecologist.

B. M. A.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

James Tyson, M.D., Professor of Medicine.

Horatio C. Wood, M.D., LL.D., Professor of Materia Medica, Pharmacy, and General Therapeutics.

Edward T. Reichert, M.D., Professor of Physiology.

Barton Cooke Hirst, M.D., Professor of Obstetrics.

J. William White, M.D., John Rhea Barton Professor of Surgery.

George A. Piersol, M.D., Professor of Anatomy.

John Marshall, M.D., Nat.Sc.D., LL.D., Professor of Chemistry and Toxicology.

Louis A. Duhring, M.D., Professor of Dermatology.

Alexander C. Abbott, M.D., Pepper Professor of Hygiene and Bacteriology.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

MALIGNANT DISEASE OF THE THYROID GLAND.

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AND

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In 1879 Kaufmann reported a series of malignant tumors of the thyroid gland, twenty-three of primary carcinoma and seven of sarcoma, fifteen of which were observed by himself and the remainder collected from the literature. Poncet, in 1889, collected fifty other cases of malignant disease from literature, comparatively recent at that time. Ehrhardt, in 1902, collected about 250 cases of both carcinoma and sarcoma and wrote an elaborate monograph upon the subject, and in this article we have made free use of his tables and deductions concerning malignant disease of the thyroid in general.

Etiology.[1] The frequency varies somewhat according to geographical location, Lücke stating that in goitrous districts the frequency of malignant disease is greater than elsewhere.

Thus, Limacher, of Berne, in 7641 autopsies found eighty-two malignant tumors (thirty-eight carcinomas, forty-four sarcomas). Hinterstoisser, of Vienna, where goitre is not markedly prevalent, found in 18,147 autopsies fifty tumors. Pick, of Prague, found eleven carcinomas and six sarcomas in 7700 postmortem examinations.

Among 7294 cases of carcinoma collected from hospitals in Great Britain, in seven instances was a primary thyroid growth recorded.

The relationship of goitre to the development of malignant disease is of great interest, particularly from the clinical aspect. While the disease is considered more prevalent in goitrous districts, Berry pertinently remarks, "That even in cases in which there is no history of pre-existing goitre it will often be found, upon examination after removal, that the tumor contains cysts, points of calcification, or some similar evidence of former disease." In five of the eight cases of carcinoma reported in this paper, either calcification or cyst formation was observed.

Ehrhardt believes that the inflammation, calcification, cystic formation, hemorrhage, and necrosis found in old goitres, whether clinically apparent or not, tend to act as chronic irritants. In the degenerated areas of the thyroid the epithelium is frequently so atypical that a diagnosis between a benign growth and early malignancy is often very difficult, and he further believes that in this atypical development lies the relation of previous disease of the thyroid to malignancy. Furthermore, Wolfler has shown that very frequently the parenchyma of the gland becomes atrophic as age advances, with a corresponding hyperplasia of the interacinous connective tissue. It is therefore possible that the production of sarcoma could be attributed to the occasional metaplasia of this tissue.

A retrosternal position of the benign struma favors retrogressive changes because during the act of deglutition the position of the goitre is changed, and this favoring alterations in the blood supply or causing trauma may bring about infarction.

Ehrhardt remarks that of 200 collected cases a history of a previous goitre was obtained in 104 (52 per cent.). In the forty-two cases collected since his paper, we found a history of previous goitre in twenty-five (59 per cent.). In thirteen of these the duration of the benign growth is specifically stated and adding these to those of Ehrhardt we find:

Duration of Previous Goitre.

Years	Cases.
1 to 10	33
10 to 20	21
20 to 30	16
30 to 40	9
40 to 50	3
	82

[1] In the discussion of the clinical aspects of malignant disease of the thyroid gland, both sarcoma and carcinoma are considered together, as it is virtually impossible in a given case to accurately distinguish between them, until the gross or microscopic appearance of the tumor has been observed.

Sex. Malignant disease of the thyroid gland (both carcinoma and sarcoma) is encountered more frequently in women (60 per cent.) than in men (40 per cent.), as is shown in the following table:

Ehrhardt's cases.		Cases collected since 1902.	
Carcinoma, females	85	Carcinoma, females	22
" males	65	" males	9
Sarcoma, females	59	Sarcoma, females	9
" males	40	" males	2

Age is an important factor, as the disease is uncommon before the age of thirty and this applies to sarcoma as well as to carcinoma, the general rule that sarcoma occurs in younger individuals not having any significance in the thyroid growths.

Years.	Carcinoma.	Sarcoma.
1 to 10	0	0
10 to 20	5	2
20 to 30	14	10
30 to 40	34	12
40 to 50	44	30
50 to 60	50	30
60 to 70	28	24
70 to 80	4	2
80 to 90	1	0

Pregnancy seems to have some influence upon the development of malignant disease of the thyroid, for in at least three cases the commencement of the growth was observed during the early months of pregnancy (Socin, Kaufmann, Frank, and Gautermann.) In three other cases a direct relationship was traced between the occurrence of trauma and the growth of the tumor (Braun, Cornil, and Sueskind). Erysipelas, influenza, and streptococcic septicæmia are also reported as having favored the development of malignancy (Schiller, Schmalbach, Gatti).

Course. In most descriptions of malignant disease of the thyroid gland both carcinoma and sarcoma are very properly considered together as it is impossible in nearly every case to distinguish between them clinically. Malignant disease may begin in either lobe, in the isthmus or when first observed may be bilateral. Of 208 cases (Ehrhardt's and our own), in 105 the right lobe, in 95 the left lobe, in 8 the isthmus were recorded as being first affected. When malignancy develops in a previous goitre the growth remains, for a longer or shorter time, circumscribed and then breaks through the capsule. In the majority of cases the tumor, from its point of origin, infiltrates the entire lobe of the thyroid and may extend across the isthmus to the other lobe, but, as has been remarked, the extracapsular growth in carcinoma especially is hindered for some time. The capsule finally becomes perforated by the growing tumor, but only at a single point at first and not diffusely.

The gross appearance and physical characteristics of malignant growths of the thyroid gland are very different in individual specimens—in size they vary from a nodule no larger than one or two centimetres in diameter up to a mass involving the entire side of the neck and extending from the jaw to the clavicle. In Cumston's case of sarcoma the growth is described as being about the size of a cherry embedded in the lower portion of a typical follicular goitre. In the case reported in this paper the sarcoma was about 3 x 4 cm. in size, surrounded by tissue typical of the thyroid gland. In advanced cases the size is greatly increased by the extracapsular growth of the tumor and by the involvement of the cervical lymph nodes. This extracapsular growth is responsible for many of the symptoms and signs of the disease, the normal anatomical relations of the various structures in the neck being considerably altered. Direct stretching may cause atrophy of the sternomastoid, sternohyoid, and sternothyroid muscles, or the growth may directly infiltrate them, as is specifically stated in the cases of Kaufmann, Wölfler, and Turner. Naturally the trachea, from its close relation with the thyroid gland, is involved to some extent in almost all of the cases and dyspnea is one of the most constant of symptoms and suffocation a frequent cause of death. The œsophagus is similarly compressed in many instances and dysphagia will be experienced.

Vinnay and Pinatelli found perforation of the trachea in 8 per cent. and perforation of the œsophagus in 4 per cent. of 173 cases. The occurrence of this accident must be attributed not only to pressure, but also to the direct invasion of the tracheal or œsophageal wall by the tumor. In one of the cases which we have observed, a perforation of the trachea nearly 2 cm. in diameter was present a short distance below the larynx.

The nerves, vagus, recurrent laryngeal, and sympathetic, are frequently surrounded by the growing tumor mass, but seem to resist the advance of the tumor into their trunk for a considerable period of time, because in but few of the reported cases was the pneumogastric directly involved except by compression and deviation from its normal course. Pressure upon this nerve is marked by cardiac disturbances upon the sympathetic by ptosis, exophthalmos, local heat, one-sided hyperæmia, etc., and upon the recurrent laryngeal by the well-known symptom of hoarseness or aphonia.

The bloodvessels are frequently compressed or distorted and especially in the case of the veins thrombosed. A number of the reported cases describe the jugular vein as being thrombosed, sometimes so extensively as to involve the entire vein from the sinus to the vena cava. At autopsy the heart clot has sometimes been reported as containing sarcoma or carcinoma cells.

In one of the cases reported in this paper an elongated tumor was found after the thyroid had been extirpated, which after ligation and excision proved to be a thrombosed jugular vein.

The cervical lymphatic nodes are involved in a large number of cases and the invasion may extend to the nodes

in the mediastinum. Braun lays especial emphasis upon the nodal involvement and believes that the increase in size of the tumor which occurs is due not only to the extracapsular extension but also to the fusion of the lymphatic nodes with the primary tumor.

Symptomatology. In discussing this phase of malignant struma we cannot refrain from first quoting the following paragraph from Berry's monograph: "When in the thyroid gland of a person over forty a tumor appears which is hard, which steadily and rapidly increases in size, and which is not of an inflammatory nature, the malignancy of such a tumor should be strongly suspected. If, moreover, the surface of the tumor is irregular and bossy, and if there is likewise dysphagia and pain in the neck, shooting up to the side of the head or to the shoulders, then the diagnosis becomes almost a certainty."

Dyspnœa and dysphagia have been previously referred to and are not of much value, except as denoting an enlargement of the gland because they are met with so frequently in benign goitre, and Berry states that the tendency of the malignant growth to infiltration of the trachea, rather than to push it aside, causes the displacement of the trachea to be less marked.

Intratracheal invasion occasionally produces hemorrhage, and this may be an early symptom, though it usually occurs late. The same invasion interfering with the tracheal blood supply may cause œdema and consequent dyspnœa, even resulting fatally from œdema of the epiglottis.

The effect of pressure upon the nerves has been referred to previously and the functional disturbances mentioned, but pain is an early symptom of importance, as it is usually absent in benign goitre. When present it is dull and neuralgic in character and is referred to the shoulder, occiput, and ear of the affected side. Tenderness on pressure is not positive in benign growths and usually present in malignant disease.

Fever of a remittent or continued type has been mentioned in some of the reported cases, and Kramer suggests that the absorption of fibrin from the degenerated foci may be the cause. He considers that in the remittent type the rise in temperature is coincident with the formation of metastases in other organs. Of course, in the presence of ulceration and suppuration fever would be present and pneumonia may occur from the tracheal ulceration.

In only about 15 per cent. of the cases reported does cachexia seem to have been considered as worthy of mention, and occurs more frequently in sarcoma than in carcinoma. In some cases, where almost the entire thyroid was involved, some of the symptoms of myxœdema have developed and the patient treated at first for this condition (Daniel). In other cases it has not been noted, and this can be explained on the assumption that either aberrant thyroid tissue becomes hyperplastic or that the colloid material in the midst of the tumor growth is sufficient for the needs of the organism.

On the other hand, it might be mentioned that Carrel-Billard found symptoms of Basedow's disease in ten of eighty-three collected cases of carcinoma of the thyroid, and Riche explains this phenomenon by pressure upon the cervical sympathetic, while Carrel-Billard believes that a hypersecretion from the proliferating epithelium is responsible for the exophthalmic goitre. Of these views the second is more probable because the tumor is rich in thyroid products and the sympathetic involvement is not demonstrable in all the cases.

Fixity of the growth to the surrounding structures, sternum, clavicle, vertebræ, muscles, etc., may prevent the movement of the thyroid during deglutition and become a valuable diagnostic sign. But the converse of this is not necessarily true, some malignant growths being quite movable.

Involvement of the lymph nodes is variously interpreted by different writers, not only for the diagnosis of malignancy but also as a means of distinguishing between sarcoma and carcinoma, because as is well known the latter affection extends so readily into the lymphatic nodes. Ehrhardt found metastasis to the lymph nodes forty-nine times in 131 cases of carcinoma and eighteen times in 107 cases of sarcoma. We have found that there is but little difference between the two tumors, at any rate not sufficient to be of any diagnostic worth, because the sarcomas gave involvement of the nodes in about 25 per cent. of cases. Berry states that the enlargement of the nodes is of no material help in the diagnosis, because those which first become affected are so deeply seated that early detection is well-nigh impossible.

Another point worthy of note is the resistance of the capsule to metastatic involvement of the nodes in carcinoma, which forces the carcinoma into portions of the very rich thyroid blood supply and favors dissemination by the circulation. It is only when extracapsular growth occurs that the lymphatic metastasis is favored.

The lymphatic metastasis takes place from the thyroid gland to the deep cervical chain of nodes, with especial involvement of those near the large bloodvessels and from there to the subclavicular, mediastinal (bronchial and cardiac), and occasionally to the axillary group. A group of nodes behind and around both the trachea and œsophagus may be involved, and occasionally the metastasis may ascend to the submaxillary and sublingual nodes. In a few instances the lymphatic tissue masses in the mucosa of the trachea and œsophagus have been noted as being involved.

Diagnosis. The diagnosis of malignant goitre is often difficult or impossible to make in the early stages, and the quotation from Berry in the section upon symptomatology can

not be too strongly emphasized. Kocher also says that a sudden increase in size in a previous goitre, either stationary or which has been growing slowly, is a characteristic symptom of malignant transformation. The sudden occurrence of hemorrhage into an old cystic cavity must of course be differentiated. Dyspnœa, dysphagia nerve disturbance, and the fixity of the growth have been fully discussed under the symptomatology, and we might add that enlargement of the subcutaneous veins in a doubtful case is of some value.

Exploratory puncture as a diagnostic aid must be strongly condemned from the danger of producing hemorrhage, infection, widespread dissemination, or involvement of the puncture tract by malignant change.

Excision of a node or a thrombosed vein can be made without danger to the patient. Hahn reports two cases in which the diagnosis was made by this means.

Malignant disease of the thyroid gland must be distinguished from benign goitre and from thyroiditis. Sufficient has been said to make plain the most important characteristics in which the former differs from malignancy.

Acute thyroiditis may arise from trauma or infection and every possible avenue for the latter must be excluded. In both malignant disease and thyroiditis a rise in temperature occurs so that this sign is of little diagnostic value. In both the nodes may appear soft, but this change occurs more rapidly in thyroiditis—they are softer, more painful, and break down more rapidly. We have previously noted the occurrence of malignant struma during the course of such infections as erysipelas, influenza, and septic infection, and this would appear to add to the difficulties. Barling reports the case of a man sixty-three years of age, operated upon for carcinoma of the thyroid in whom a suppurative strumitis only was found, and Cumston mentions a simple strumitis following typhoid infection which was removed because of the diagnosis of possible malignant transformation.

Laryngoscopic examination is often of value, revealing hyperæmia, œdema, and paralysis of the vocal cords. The latter observation in the presence of the history of a goitre makes the diagnosis of malignancy probable with a fair degree of certainty. Ulceration of the trachea is diagnosed by the appearance of bloody sputum and occasionally by the expectoration of small pieces of tumor. In a case reported by Ehrhardt bloody sputum was the only symptom present.

HISTOLOGY OF MALIGNANT GOITRE.

Carcinoma. Primary carcinoma of the thyroid gland appears in the form of the medullary, scirrhus, and squamous epithelial types; and of these three the medullary, which can occur as an adenocarcinoma or cylindrical-cell cancer, is by far the most common. The diagnosis of this form may be made macroscopically, the grayish-white cut surface, the dryness of the tissues, and the small amount of blood contrasting strikingly with the yellow-red, succulent, and translucent appearance of a benign struma. Microscopically the structure is decidedly alveolar in arrangement, the compact cancerous alveoli lie in a stroma which is usually poor in cells and varying in amount.

Adenocarcinoma may not be distinguished grossly from a benign growth, the color and consistency being similar. This form can be considered according to Ehrhardt in two groups: the cylindrical cell and adenocarcinoma. The former occurs in the thyroid as long drawn-out tubules lined by several layers of epithelium, and is characterized by a tendency to form sprout-like processes or distinct papillæ. The tunica propria is absent and the secretion of the cells resembles colloid macroscopically and by its staining reactions. To explain the presence of cylindrical epithelium in an organ which never in its existence contains such a structure, Ehrhardt believes a metaplasia must have taken place, the normal cuboidal cells being thus changed into a cylindrical variety. The papillary cyst-adenomata are frequently placed in a class between benign and malignant growths. In general they grow slowly, the degree of malignancy is not pronounced, the tendency to infiltrate surrounding parts or to form metastases is small, and liability to recurrence is not great. For these reasons this variety is very amenable to treatment. Of six cases reported by Low, two showed evidences of malignant change, while out of four under the authors' observance, two likewise had undergone carcinomatous degeneration.

The adenocarcinoma may for a long time remain unnoticed, because the enlargement may not be apparent. The nature of the tumor, in fact, has first been recognized by its metastasis. The tendency of this variety of thyroid carcinoma to cause solitary bone metastasis is striking, while the slow growth of the secondary tumor is often of clinical significance. While, in general, surgeons do not operate upon bone metastases, yet this variety offers hope because of the slow growth, the solitary foci and the usual freedom from pulmonary involvement. In the histological examination of these cases particular care must be observed, for instances are recorded in which malignancy was discovered after the microscopic diagnosis of adenoma had been made. The diagnosis of adenoma should only be made when the entire tumor has been subjected to a careful examination and the indications of malignancy excluded: Absence of a tunica propria, growth into neighboring organs and especially veins, multiple layers of epithelial cases, and cylindrical cell lining of the gland tubules.

Scirrhus cancer of the thyroid is rare and may be seen in young individuals. Enlargement of the gland may be absent and in that event the process is characterized by the

hardness of the growth. The lymph nodes are involved early in the course of the disease. The thyroid macroscopically is small, its substance hard, and creaks on cutting. At the periphery carcinomatous cells can be demonstrated microscopically, while toward the centre is found a hard, fibrous mass resembling scar tissue, in which here and there remains of necrotic gland tissue are seen. The picture corresponds to the cicatrizing scirrhus cancer of the breast, the patient suffers from gradually increasing pain radiating in character, difficulty in breathing and swallowing. The latter may appear early and cause symptoms of œsophageal stricture. Metastasis is not known, the prognosis therefore, being good and early operative interference being indicated for the same reason.

Squamous carcinoma develops slowly and in many of the reported cases metastasis did not arise. From the cut surface small drops resembling comedo may be expressed, and microscopically prickle cells and pearly bodies are present. It is not likely that the squamous epithelium is the result of a metaplasia, but probably arises from inclusions of the integument during fetal life or from epithelial remnants of the branchial cleft.

Sarcoma. Morf (1899) collected forty-one reported cases of this disease—Lartigau (1901) added fifteen more—and Ehrhardt (1902), with the advantage of access to inaugural dissertations, reported about 100 cases. Since the publication of Ehrhardt's paper eleven additional cases have been recorded in the literature, viz.:

Analysis of Eleven Cases Reported Since 1902.

Reporter.	Year.	Sex.	Age.	Microscopic variety.	Result.
1. Daniel	1902	M.	57	Round cell	Death
2. Daniel	1902	M.	59	" "	Death
3. Daniel	1902	F.	69	" "	Death
4. Daniel	1902	F.	60	" "	Death
5. Funkenstein	1903	F.	62	Osteochondrosarcoma.	Death
6. Colby	1904	F.	67	Round cell	Death
7. Kaufmann	1904	F.	56	"Sarcoma"	Death
8. Papin and Saboreanu	1904	F.	27	Spindle cell	Death
9. Botella	1905	F.	41	Fibrosarcoma	Recovery
10. Syme	1905	F.	53	Mixed cell	Death
11. Muller and Speese	1906	F.	50	Spindle cell	Death

Females, 82 per cent. / Males, 18 per cent. = average age fifty-five years. Mortality, 91 per cent.

In this country primary sarcoma of the thyroid gland must be considered as a rare affection, as but eleven cases have been recorded in the literature.

Analysis of Eleven Cases Reported in U. S. A.

Reporter.	Year.	Sex.	Age.	Microscopic variety.	Result
* 1. Bryant	1891	M.	56	Round cell	Death
* 2. Graham	1893	M.	60	Round cell	Death
* 3. Allen	1897	F.	22	Round cell	Death
4. Tiffany and Lanier	1897	F.	66	Spindle cell	Death
* 5. Berkeley	1898	F.	47	Angiosarcoma	Recovery
* 6. Stengel	1898	M.	30	Round cell	Death
7. Morf	1899	M.	47	Mixed, round & spindle	Death
* 8. Cumston	1899	F.	47	Spindle cell	Recovery
9. Lartigau	1901	F.	45	Angiosarcoma	Death
*10. Colby	1904	F.	67	Round cell	Death
*11. Muller and Speese	1906	F.	50	Spindle cell	Death

Females, 64 per cent. / Males, 46 per cent. = Average age, forty-nine years. Mortality, 82 per cent.

* Not included in Ehrhardt's bibliography

There is but little to add to the general description already given. The skin over the growth may or may not be adherent and is sometimes involved by the sarcoma process to such an extent as to break down and result in a sloughing fungus mass upon the side of the neck, as in the cases reported by Gatti and Jones and Battle.

When removed and split open the surface of a sarcoma varies from a red fleshy looking growth, as in the lymphosarcomata and some of the round-cell forms, to the more usual white or yellowish-white, smooth, fibrous-like surface, with numerous trabeculæ and prolongations into the surrounding gland. In the angiosarcomata, as in Lartigau's case, the color may be a dark red with lighter yellow areas. The majority of the reported instances are examples of the round- or spindle-cell forms or a "mixed" type composed of round- and spindle-cells, sometimes giant cells.

The following are the chief varieties noted in the appended list of 117 cases, in 97 of which the form is noted:

1. Spindle-cell sarcoma	30	
2. Round-cell sarcoma	22	
3. Mixed-cell sarcoma	16	
	68	(70 p. c.)
4. Angiosarcoma	8	
5. Fibrosarcoma	5	
6. Lymphosarcoma	4	
7. Melanosarcoma	2*	
8. Giant-cell sarcoma	2	
9. Myxosarcitoma	2	

* Colby's case is doubtful.

The round- and spindle-cell sarcomas are rarely sharply encapsulated, mostly diffusing themselves and infiltrating one or more lobes of the thyroid gland.

The case which we report follows the rule emphasized by Kaufmann and others that most of these sarcomas, and especially the spindle-cell variety, grow from the interacinous connective tissue and then infiltrating between the follicles, widely separate them, and complete their destruction by a pressure atrophy.

The colloid substance may be present amidst the tumor tissue without trace of the epithelium, either as an escaping secretion or formed from areas of hemorrhage.

Among the round-cell sarcomas may be placed the lymphosarcomas, with their similarity in structure to the lymphoid tissue, and those classed as giant-cell growths which were usually mixed types with numerous large polynuclear cells.

The fibrosarcomata are essentially spindle-cell forms in which the fibrillation of the cells bespeaks for a lessened degree of malignancy, although from our own observation of the reported cases there seems to be no relation between the type of tumor and the death or recovery of the patient.

A number of the tumors, especially those of older date, are reported as "cystic sarcomas," and either existed previously to the malignant change or were probably dilated lymph spaces. As would be expected from the vascular richness

of the thyroid gland a number of the sarcomas are classed as angiosarcoma, cavernous sarcoma, endothelioma, etc. Whether these were simply dilated and elongated capillary vessels, involved in the malignant connective tissue, proliferating endothelium or perithelium, or whether they were true angiomata it is impossible to state, but probably they were all endotheliomas with vessel richness.

The well-known tendency of old goitres to undergo calcification has given rise to some discussion as to whether the reported cases of osteosarcoma of the thyroid were really such or whether true bone-formation had occurred. Forster, Maier, Parsons, Lucke, Tenoin and Pilliet, Pick, Ehrhardt and Funkenstein have reported such tumors, although most of the cases are probably instances of calcification of the fibrous tissue resembling bone. Other observers, Lentz and Reverdin and Buscarlet for instance, report chondrosarcomas.

A few curious cases have been reported (Kaufmann, Kummer, Syme) where both carcinoma and sarcoma were present in the thyroid, the cause of which cannot even be surmised. Botella's case of sarcoma is described as having some areas resembling tuberculosis.

The characteristics of thyroid sarcomas are less difficult of demonstration than carcinoma and follow the usual descriptions of these growths. The metastasis to the lymph nodes and other organs has been fully discussed.

Metastasis. According to Ehrhardt, metastasis is observed in eighty-five per cent. of the reported cases of malignant goitre where an exact autopsy record exists. Of these, 50 per cent. of the carcinomas gave metastasis by way of the bloodvessels alone, and 20 per cent. of the sarcomas disseminated the tumor solely through the lymphatic channels. This is interesting in view of the usual methods of dissemination and the reason therefor. In the case of the carcinomas it has been mentioned elsewhere, as has also the method of metastasis to the lymphatic nodes.

In 238 cases collected by Ehrhardt, and to which we have added nineteen, the following organs and structures were reported as being the seat of the metastasis:

	Carcinoma.	Sarcoma.
Bones	49	24
Lung	72	65
Liver	5	16
Kidney	14	10
Brain	7	5
Pleura	12	6
Myocardium	1	4
Adrenal	2	1
Pericardium	1	0
Spleen	0	1
Omentum	3	0
Intestine	1	2
Ovary	1	0
Mamma	1	0
Stomach	1	1
Diaphragm	1	0
Pancreas	0	1

From the above table it can readily be seen that the lung is the most frequent seat for metastatic growths (48 per cent. sarcoma, 42 per cent. in carcinoma) and that bone is the second site of prevalence (carcinoma 29 per cent. sarcoma 18 per cent.).

These figures are somewhat at variance with the observation of Limacher, who found that bone was involved more frequently than the lung in carcinoma of the thyroid.

Metastasis to bone is not only a frequent but a very interesting complication of these malignant thyroid tumors, because this organ together with the breast and the prostate are practically the only ones in which metastasis to bone is commonly observed. It is difficult to understand why these organs have a predilection for the bone-marrow unless one accepts v. Recklinghausen's theory that the sluggishness of the blood current in the wide venous capillaries favors the formation of mural thrombi by corpuscular elements; but this does not explain why carcinoma of the stomach or uterus, for instance, does not affect the bones more often. Another peculiarity is the frequent presence in the metastatic bone tumor of colloid material contained in normal or abnormal vesicles, in practically all cases, of course, the primary tumor being a carcinoma not a sarcoma.

Clinically the myelogenous metastases may not be manifest until spontaneous fracture occurs, and contrary to the opinion of many writers Ehrhardt believes that union of the fragments may readily occur because of the abundant osteophytic formation.

The influence of the thyroid gland upon fractures in general and the production of thyroid tissue in bone in cases of simple benign struma, while intensely interesting, cannot be discussed in this paper.

The following table (65 cases collected by Ehrhardt, to which we have added ten more) shows the particular bones involved:

	Cases.
Skull	31
Inferior maxilla	30
Sternum	18
Vertebra	16
Rib	12
Femur	11
Humerus	10
Pelvis	9
Scapula	4
Zygoma	3
Clavicle	1
Palate	1

v. Eiselsberg has called especial attention to the formation of solitary bone metastases in adenocarcinoma of the thyroid, and it has also been noted that in this variety of tumor the tendency is very slight to lung metastases, and so in a given case the complete eradication of the primary tumor would not, if followed by a spontaneous fracture, of necessity mean that the prognosis must be absolutely bad.

TABLE I.—CASES OF CARCINOMA OF THE THYROID REPORTED SINCE 1902.

Author.	Sex.	Age.	Previous goitre.	Lobe affected.	Histological diagnosis.	Result.	Metastasis.
1. Kaufmann.	F.	63	Present.	... ...	Adenocarcinoma.	Death.	Femora, rib, vertebra, lung.
2. Lebhardt and Saltykow.	F.	42	... ...	Right.	Adenocarcinoma.	Tracheotomy and death.	Liver, kidney, omentum, colon serosa, ovary.
3. Saltykow.	F.	73	... ...	Right and middle.	Not made.	Death.	Pelvis, lung.
4. de Graag.	F.	56	Present eight years.	Right.	Adenocarcinoma.	Ulceration of trachea; death.	Vertebra, lung, pleura.
5. Huguenin.	M.	58	... ...	Left	Adenocarcinoma, 4 mm. in diameter.	Death following operation.	Vertebra.
6. Chartier.	M.	74	Present several years	Right.	Squamous carcinoma.	Death; ulceration of œsophagus.	No metastasis.
7. Zipkin.	M.	65	... ...	Left.	Adenocarcinoma.	Death.	Lungs, pleuræ, bronchial nodes, diaphragm.
8. Faisant.	M.	47	Present.	Left, extension to right.	Cancer.	Not stated.	Adherent to sternomastoid and œsophagus.
9. Lesieur and Dumas.	M.	69	Present.	Left.	Adenocarcinoma.	Death.	Stomach perigastric nodes.
10. Lediard.	F.	62	Present several years.	... ...	Adenocarcinoma.	Death.	Skull.
11. Syme.	F.	53	... ...	Left.	Scirrhus carcinoma; sarcoma.	Paralysis of vocal cord; death.	Ulceration of trachea and œsophagus.
12. Downie.	M.	61	... ...	Left.	Squamous carcinoma.	Death.	Liver, trachea and œsophagus adherent.
13. Delore.	F.	54	Present two years.	Left.	Cancer.	Death; ulceration of trachea and œsophagus.	Lung, cervical nodes.
14 "	F.	53	Present.	Left.	Cancer.	Operation, recurrence and death.	Vertebra, clavicle, mamma.
15. "	F.	50	Present.	Left.	Cancer.	Recurrence in 6 years; death.	Adhesions to vessels and nerves; ulceration of trachea.
16. "	M.	57	... ...	Right.	... ...	Inoperable; death.	
17. "	F.	56	Present.	Right.	... ...	Pressure on sympathetic; recurrence following operation.	
18. "	F.	64	Present several years.	Left.	Cancer.	Death; ulceration of trachea.	
19. "	F.	57	Present.	Middle.	Cancer.	Death.	
20. "	F.	51	Present.	Left.	Cancer.	Recurrence; death.	Lung.
21. "	F.	65	Present.	Right.	Adenocarcinoma.	No recurrence 15 mos. after operation.	
22. Low.	F.	40	Present.	Right.	Papillary cystadenoma, with malignant change.	Not stated.	
23. "	F.	18	Present.	Right.	Papillary cystadenoma, with malignant change.	Not stated.	
24. Muller and Speese.	F.	48	Present 16 years.	Right.	Adenocarcinoma.	Operation, recovery, history of recurrence not known.	
25. " "	F.	34	" 17 "	... ...	Adenocarcinoma.	Operation successful; further history not known.	
26. " "	F.	18	" 3 "	Left.	Carcinomatous degeneration of a cystic goitre.	Immediate result good.	
27. " "	M.	66	" 25 "	Right.	Adenocarcinoma.	Death in one day; thrombosis of jugular present.	
28. " "	F.	25	" 4 "	Left.	Papillary cystadenoma.	No recurrence 18 mos. after operation.	
29. " "	M.	40	... ...	Left.	Adenocarcinoma.	Death.	
30. " "	F.	...	... ...	Right.	Adenocarcinoma.	... ...	
31. " "	F.	48	... ...	... .	Papillary cystadenoma.	... ...	

TABLE II.—117 CASES OF SARCOMA OF THE THYROID GLAND COLLECTED FROM THE LITERATURE.

Reported by	Sex.	Age.	Previous goitre.	Lobe affected and duration of acute symptoms.	Glandular involvement.	Microscopic variety.	Result.	Points of interest.
1. Albert, 1882.	M	41	Four years.	R. two months.	...	Spindle cell.	Death.	Died two months later.
2. Allen, 1897	F	22	None.	R. two years.	..	Round cell.	Death.	Operation; died five hours later from shock
3. Berkeley, 1898.	F	47	Sixteen years.	M. two years	...	Angiosarcoma.	Recovery.	
4. Berry, 1901.	F.	50	... ...	R.	... ...	Spindle cell.	Death.	Recurrence four months after operation.
5. Berry, 1901.	M	25	.. . .	L. three months	. .	Spindle cell.	Death.	Inoperable; died from hemorrhage; no metastasis.
6. Berry, 1901.	F	53	Forty years.	R. four months	. .	Spindle cell.	Death.	Died eight months later from onset of acute symptoms; inoperable.
7. Boeckel.	F.	48	Ten years.	L.	...	Giant cell.	Recovery.	Recurred in supraclavicular glands three years later; removed; recovery.
8. Botella, 1905	F.	41	... .	M. five months.	. .. ...	Fibrosarcoma.	Recovery.	Some areas resembled tuberculosis microscopically.
9. Bowlby, 1885.	F.	42	... .	B. three years.	None.	Fibrosarcoma.	Death.	Died from suffocation after tracheotomy two months later.
10. Bircher, 1884.	M.	50	None.	... .	Involved.	Round cell.	Death.	Metastasis in lungs.
11. Braun, 1879.	F.	59	Twenty years.	L. four months	Involved.	Lymphosarcoma.	... ...	
12. Braun, 1879.	M.	59	Many years.	R.	Involved.	Round and spindle.	Death.	Metastasis to left ventricle; fifth costal cartilage; perichondrium; pleura; left lung and liver.
13. Braun, 1879.	F.	46	Twenty-nine years	... ...	Involved.	Cavernous.	Death.	Metastasis to lungs.
14. Braun, 1879.	F.	44	Ten years.	... .	Not involved.	Spindle cell.	Death.	Fatal hemorrhage.
15. Braun, 1879.	M.	58	Twenty-four years.	R.	Involved.	Vascular round cell.	Death.	Metastasis to right lung and seventh cervical vertebra.
16. Bryant, 1891.	M.	56	None.	R. three months.	.. ..	Round cell.	... ...	Operation; growth only partly removed; two weeks later was cachectic and failing.
17. Cumston, 1899.	F.	47	Eighteen months.	L. ten weeks.	... ...	Spindle cell.	Recovery.	Operation; removal of lobe.
18. Colby, 1901.	F.	67	Eleven years.	R. two years.	... ...	Pigmented large round cell	Death.	No autopsy; death in two months.
19. Daniel, 1902.	M.	57	... ...	R. twelve months.	... ...	Giant cells and round cell.	Death.	Died after tracheotomy; no visceral lesions.
20. Daniel, 1902.	M.	59	. ...	B. eight months.	... .	Round cell.	Death.	Syncope; twelve days after tracheotomy metastasis to lower dorsal vertebra; retroaortic glands; both kidneys; both suprarenals.
21. Daniel, 1902.	F.	69	... ...	M. nine months.	... ...	Round cell.	Death.	Died five days after operation; metastasis to both kidneys.
22. Daniel, 1902.	F.	60	.. ...	L. seventeen months (then R.)	Involved, especially L.	Round cell.	Death.	Died eighteen months from beginning; patient had characteristic symptoms of myxedema; metastasis to pancreas; stomach(?); ileum (?)
23. Ehrhardt, 1902.	F.	65	Two years.	B.	Not involved.	Lymphosarcoma	Death.	Died five days after operation; bronchopneumonia.
24. Ehrhardt, 1902.	F.	16	... ...	Four weeks.	Involved.	Lymphosarcoma	Death.	Suffocation.
25. Ehrhardt, 1902.	F.	33	... ...	R. seven months.	... ...	Lymphosarcoma.	Death.	Died five weeks after operation; tetany.
26. Ehrhardt, 1902.	F.	54	Ten years.	(retrosternal) L. four months.	... ...	Small round cell.	Recovery.	Operation; "shelled out."
27. Ehrhardt, 1902.	M.	33	... ...	L. two months.	... ...	Giant cell.	Death.	Forty-three days after operation, at which complete removal was impossible; metastasis to lungs; pleura; liver; perforation of pharynx, oesophagus and trachea.
28. Ehrhardt, 1902.	F.	21	... .	R. four years.	... .	Small round cell (osteoid sarcoma).	Death.	Recovered from primary operation; five years later pain developed in right hip with shortening; sixteen months later a pathologic fracture occurred and a portion of the tumor revealed an endothelioma similar in structure to the original thyroid growth.
29. Firth, 1899.	F.	69	... ...	B. three months.	Involved.	Mixed, small and spindle cell.	Recovery.	Recovery from operation, but growth was not entirely removed.
30. Fraenkel, 1897.	F.	49	... ...	L.	Involved.	Melanosarcoma.	Death.	Metastasis to liver; subcutaneous tissues back and chest; lymph nodes of neck and axilla; bones of skull, sternum, left femur; pleura; lungs; head; pancreas; kidney; adrenals.
31. Funkenstein, 1903.	F.	62	Many years.	... .	... .	Osteochondrosarcoma.	Death.	Died three weeks after operation; metastasis to lungs.
32. Forster, 1869.	F.	60	... .	R.	None.	Spindle cell (bony tissue)		
33. Gatti, 1895.	M.	40	Since childhood.	R.	... .	"Polymorphous" Giant, large and medium-size cells.	Death.	Metastasis to lungs; duration of disease, seven months; death from suppuration.
34. Graham, 1903.	M.	60	Two years.	... ...	.. ...	Round cell.	Death.	Cerebral embolus; duration of disease, five months.
35. Heath, 1879.	F.	55	... ...	R.	. ...	Spindle, round and "mixed" cells.	Death.	Metastasis to pleura and lung; duration of disease, about six months.

TABLE II.—Continued.

Reported by	Sex.	Age.	Previous goitre.	Origin.	Glandular involvement.	Microscopic variety.	Result.	Points of interest.
36. Heddinger, 1901.	F.	51	... ...	... ...	... ...	Mixed, round and spindle.	Death.	Metastasis to heart and lung.
37. Heddinger, 1901.	F.	64	... ...	B.	... ...	Small, round cell.	Death.	
38. Heddinger, 1901.	F.	..	... ...	... ...	... ...	Spindle cell.	... ...	
39. Heddinger, 1901.	M.	37	Some time.	Three weeks.	... ...	Spindle cell.	... ...	
40 Heddinger, 1901.	.	...	... ...	... ...	... ...	Spindle cell.	... ...	
41. Heddinger, 1901.	.	51	Six months.	... ...	... ...	Mixed, round and spindle.	... ...	
42. Heddinger, 1901.		60	... ...	... ...	... ...	Spindle cell.	Death.	Metastasis to pleura and lung.
43. Jones and Battle, 1898.	M.	42	Five years.	R. few months.	... ...	Spindle cell.	Death.	Operated; recurred in sixteen weeks; several operations and recurrence; death nine months after the first operation.
44. Kaufmann, 1879.	M.	66	Long time.	... ...	Involved.	Spindle cell.	Death.	Metastasis to pleura.
45. Kaufmann, 1879.	F.	55	Since youth.	... ...	... ...	Spindle cell.	Death.	Metastasis to anterior mediastinum; both lungs; liver.
46. Kaufmann, 1879.	F.	46	Three years.	L. (?)	... ...	Cystosarcoma.	... ...	
47 Kaufmann, 1879.	M.	56	Long time.	L.	... ...	Small, round cell.	Death.	Mediastinal lymph glands
48. Kaufmann, 1879.	F.	61	None.	L.	... ...	Round cell.	Death.	No metastases.
49. Kaufmann, 1879.	M.	54	... ...	... ...	... ...	Spindle cell.	Death.	Metastasis to bones; muscles; skin.
50. Kaufmann, 1879.	F.	57	None.	R.	... ...	Mixed, round and spindle.	Death.	No metastasis; duration, five months.
51. Kaufmann, 1904.	F.	56	... ...	... ...	... ...	Sarcoma.	Death.	Metastasis to lung; heart; kidney.
52. Kohler, 1887.	M.	43	Twelve years.	L.	... ...	Round cell.	Death	Hemorrhage and collapse after operation; metastasis to lungs and kidneys.
53. Kummer, 1898.	F.	55	... ...	L.	... ...	"Adenosarcoma."	Death.	No autopsy.
54. Kobler, 1886.	M.	62	None.	R.	Involved.	Spindle cell.	Death.	Cerebral hemorrhages.
55 Labbe, 1895.	M.	44	Six years.	R three months.	... ...	Round cell.	Death.	Asthenia.
56. Lartigau, 1901.	F.	45	Eight years.	R. ten days.	Not involved.	Angiosarcoma.	Death.	Died from asphyxia sixteen days after operation; no metastasis; recurrence at site.
57. Lentz, 1893.	F.	56	Forty years.	L.	... ...	Chondrosarcoma, spindle cells.	... ..	
58. Limacher, 1898.	F.	59	Many years.	R.	Involved.	Alveolar sarcoma (angiosarcoma).	Death.	Metastasis to lungs; sternum; duration, eight months; arose from endothelium of blood-vessels.
59. Limacher, 1898.	M.	49	Many years.	... .	... ...	Angiosarcoma.	... ...	
60. Maas, 1880.	M.	68	... ...	R.	... ...	Mixed, round and spindle.	Death.	Asthenia; no autopsy.
61. Moore, 1877.	F.	46	... ...	R. four months	... ...	Spindle cells.	Death.	Metastasis to kidneys; rib; brain.
62. Maier, 1877.	F.	40	... ...	... ...	... ...	Mixed (round, spindle, bone and cartilage.)	... ...	In some areas large epithelial-like cells suggest carcinoma.
63. Morf, 1899.	M.	47	None.	R. one year.	None.	Mixed, round and spindle.	Death.	Operation; recurrence in five months; death; metastasis to lungs.
64. Mathieu, 1881.	F.	69	None.	... ...	Involved.	Round cell.	... ...	
65. Neumann, 1879.	F.	54	Five years.	... ...	... ...	Alveolar sarcoma, with colloid masses.	... ...	Metastasis to humerus.
66. Paget, 1887.	F.	50	Thirty years.	L. six weeks.	.. ..	Round cell.	Death.	Suffocation.
67. Papin and Sabourin, 1904.	F.	27	Four years.	R.	... ...	Spindle cell.	Death.	Suffocation.
68. Pick, 1892.	F.	51	Many years.	L.	Involved.	Spindle cell (and bony tissue).	Death.	Duration of disease, about one year; metastasis to lungs; heart; liver; stomach; intestines; pancreas; dura mater; palate
69. Pitt, 1887.	M.	69	None.	L.	Involved.	Round cell.	Death.	Duration of disease, four weeks.
70. Rabe, 1897.	M.	39	... ...	L. eight months.	... ...	Mixed, round and spindle.	Death.	No metastasis.
71. Reverdin & Buscarlet, 1897.	F.	63	... ...	R.	... ...	Spindle cell (cartilage).	Death.	Operation; died twenty-four hours later from shock.
72. Rose, 1879.	F.	36	... ...	L. M.	... ...	Medullary sarcoma.	Death.	Died after explorative operation; metastasis to lungs and mediastinal nodes.
73. Rose, 1879.	M.	53	Many years.	M.	... ...	Spindle cell.	Death.	Metastasis to mediastinal nodes; lungs; heart; liver.
74. Rose, 1879.	F.	46	Four years.	L. four months.	... ...	Sarcoma.	Death.	Operation; died thirteen days later; no metastasis.
75. Rotter, 1885.	M.	68	... ...	R.	... ...	Mixed (round and spindle).	Death.	Operation; tracheotomy; death; no autopsy.
76. Roux, 1891.	F	70	... ...	R.	... ...	Small, round cell.	Recovery.	

TABLE II.—Continued.

Reported by	Sex	Age.	Previous goitre.	Origin.	Glandular Involvement	Microscopic variety.	Result	Points of interest.
77. Roux, 1891.	M.	59	... .	L.	..	Fibrosarcoma.	.. .	
78. Roux, 1891.	M.	50	Many years.	R. six months.	. ..	Sarcoma.	Death.	Operation; hemorrhage.
79. Roux, 1891.	M.	33	... ...	M.	Involved.	Sarcoma.	Recovery	
80. Shattock, 1888.	M.	42	... .	R. five years.	... ...	Spindle cell.	Death	Operation five times for recurrence; died ten months after the first operation; compensatory hypertrophy of an outlying lobule.
81. Sieveking, 1894.	M.	42	...	Three months.	Involved.	Small, round cell.	Death	Metastasis to heart, liver, intestines, kidney bone-marrow, omentum.
82. Stengel, 1898.	M.	30	... .	Three months.	.. . ...	Round cell.	Death.	Metastasis to lungs.
83. Syme, 1905.	F.	58	Years.	L. one month.	... .	Mixed sarcoma and scirrhus cancer.	Death	Tracheotomy; died ten days later.
84. Schiller, 1899.	F.	23	Thirteen years.	R.	... .	Sarcoma.	Death.	Operation; no metastasis.
85. Schiller, 1899.	M.	24	Five years.	R.	... .	Cystic sarcoma.	Recovery	Could not be traced seven years later.
86. Schiller, 1899.	F.	42	Long time.	L.	... .	Cystic sarcoma.	Recovery	Could not be traced seven years later.
87. Schiller, 1899.	F.	51	Twelve years.	Six weeks.	.. ...	Sarcoma.	Death	Operation; recurrence; died two months later from hemorrhage.
88. Schiller, 1899.	M.	41	Twenty-three years.	R. one week.	Involved.	Sarcoma.	Death.	Operation; recurrence in scar, axillary and cervical glands, died four and a half years later from pulmonary hemorrhage.
89. Schiller, 1899.	M.	18	Since childhood.	L. three months	... .	Myxosarcoma.	Recovery.	Operation; not traced six years later.
90. Schiller, 1899.	M	59	Two years.	L. ten weeks.	Involved.	Myxosarcoma.	Death	Operation; recurrence; died five weeks later.
91. Schiller, 1899.	F	60	Forty-six years.	R. several months.	... .	Sarcoma.	Death	Operation; recurrence; died four months later from suffocation.
92. Schiller, 1899.	F.	37	Three years.	R. lately rapid	... ...	Angiosarcoma	Recovery	Operation; no recurrence five years later.
93. Schiller, 1899.	M.	...	... ...	L.	... ...	Cystic sarcoma.	Death.	Operation; died four months later with recurrence.
94. Schiller, 1899.	M.	20	Four years.	L. lately rapid.	... .	Endothelioma.	Recovery	Operation; no recurrence five years later.
95. Schiller, 1899.	M.	41	Fourteen years	L. two months.	... .	Sarcoma.	Death.	Operation; recurrence; died two months later.
96. Schiller, 1899.	F.	40	Nine years.	R. two weeks.	... .	Sarcoma.	Death.	Operation; died in two months; at autopsy the jugular was involved; no metastasis.
97. Schiller, 1899.	F.	53	Forty-seven years.	B. lately rapid.	Involved.	Cystic sarcoma.	Death.	Operation; died in twenty-four hours from pulmonary œdema.
98. Schiller, 1899.	F.	19	Three years.	Gradual.	... ...	Cystic sarcoma.	Recovery.	Operation; no recurrence four years later.
99. Schiller, 1899.	F.	71	... ...	R. five weeks.	... ...	Cystic sarcoma.	Death.	Operation; recurrence; died five months later.
100. Schiller, 1899.	M.	55	... ...	R. one year.	.. ..	Spindle cell.	Recovery.	Operation; not traced three years later.
101. Schiller, 1899.	F.	46	Long standing.	R six months	... .	Sarcoma.	Death.	Operation; died one-half hour later; walnut-size nodule in superior vena cava.
102. Schiller, 1899.	M.	65	.. ..	L. three months.	... ...	Cystic sarcoma.	Death.	Operation; recurrence; died in six months.
103. Schiller, 1899.	M.	51	... ...	B. three months	Involved.	Spindle cell.	Death.	Operation; not entirely removed; died in two months; pneumonia and hemorrhage; metastasis to lungs and nodes.
104. Schiller, 1899.	F.	23	... ...	... ...	... .	Small, round cell.	Recovery	Operation; no recurrence in three years. (Note—Growth was in an aberrant thyroid.)
105. Schiller, 1899.	M.	31	... ...	L.	... ...	Spindle cell.	Death.	Operation; recurrence; died in ten months.
106. Scheiber, 1872.	M.	40	Years.	R.	Involved.	Alveolar sarcoma.	Death.	Metastasis to cranial bones.
107. Schumziger, 1882.	M.	49	Many years.	R.	... ...	Mixed (round and spindle cell).	... ...	
108. Tiffany and Lanier, 1897.	F.	66	... ...	R. one year.	... ...	Spindle cell.	Death.	No autopsy.
109. Tilleaux, 1881.	M.	33	None.	... ...	None.	Fibrosarcoma.	... ...	Clinical symptoms and signs of Basedow's disease.
110. Turner, 1890.	F.	66	... ...	Nine months	None.	Round cell.	... ..	Sternomastoid infiltrated.
111. Thorl, 1865.	F.	46	Seventeen years.	... ...	... ...	Cystic sarcoma.	... ...	
112. Wolfler, 1883.	M.	38	Fifteen years.	R. ten weeks.	Involved.	Fibrosarcoma.	... ...	
113. Wolfler, 1883.	M.	51	Nineteen years.	R.	Involved.	Angiosarcoma.	Death.	Pulmonary œdema; metastasis to lungs; left ilium; mediastinal nodes.
114. Wolfler, 1883.	M.	63	None.	R. four months.	... ...	Round cell.	... ...	
115. Wolfler, 1883.	F.	51	... ...	L.	... .	Mixed (round, spindle and giant cells).	Death.	Tumor thrombus in jugular vein; metastasis to dura.
116. Wolfler, 1883.	F.	35	... ...	... ...	.. ...	Alveolar angio-sarcoma.	... ...	
117. Muller and Speese, 1906.	F.	50	None.	R. fourteen months. Gradual.	Involved.	Spindle cell.	Death.	Operation; recurrence; second operation one year later; recurrence; died three and a half years from beginning of disease; metastasis to liver.

Jäger has classified the possibility of metastases according to the microscopic findings, as follows:

1. Cases of metastatic malignant struma in which normal thyroid tissue is present.

2. Cases in which metastasis of an apparently benign struma contains carcinomatous tissue.

3. Cases in which it is difficult to say from the metastasis whether the struma is benign or not.

4. Cases of metastatic benign tumors in which carcinomatous tissue could not be recognized.

Prognosis. The course of malignant disease of the thyroid is on the whole rapid and the prognosis distinctly grave. It is difficult to accurately state the duration of the disease because the transition from the previous benign growth to the malignant one is rarely sharply marked. Rose has placed the limit of duration at nine weeks and eighteen months, although a number of cases are on record in which variation from this time has been noted. While no real difference exists between carcinoma and sarcoma in general, yet it may be stated that the acute forms are seen more commonly in sarcoma and the chronic ones in carcinoma.

Suffocation from pressure upon the trachea and pneumonia from the same cause, with lung infection, are the principal causes of death. Cachexia is observed most frequently in those cases where the primary growth is small and metastasis considerable. Hemorrhage, œdema of the glottis, starvation, and suppuration of the tumor are also causes. Sudden hemorrhage into the tumor may cause death by pressure.

The exact percentage of mortality is almost impossible to compute because of the inaccuracy or rather incompleteness of most of the reported cases. We can state, however, that the mortality, including both the operative mortality and the deaths from a speedy recurrence within a few months, should be placed at 70 per cent. *at least*. Of the 42 cases collected since 1902, in 30, or 71 per cent., a fatal termination is noted, while of 9 no further mention is made. It is presumed that Cumston's case recovered and Delore reports that his case, fifteen months after operation, is free from recurrence. Case V. in the present paper is living and free from recurrence eighteen months after operation. The mortality figures in Tables I. and II. present a startling unanimity of results and make malignant disease of the thyroid gland a very grave disease.

The operative treatment of the disease will not be discussed. The following conclusions would seem to be justified by our study:

1. Malignant disease of the thyroid gland is not a common affection, particularly in this country, where only eleven sarcomas have been recorded.

2. It is encountered more frequently in women (three to two) and the greater number of cases (53 per cent.) occur between the ages of forty to sixty. Only 11 per cent. of the sarcomas occurred in patients under the age of thirty.

3. In 53 per cent. of cases a history of a previous goitre will be obtained, which in over half the cases is of more than ten years' duration.

4. Adenocarcinoma and the round- and spindle-cell sarcomas are the most frequent types of tumor. Papillary cystadenocarcinoma is the least malignant form of carcinoma and presents the most favorable prognosis.

5. The metastasis involves the lungs and bones most commonly and of the latter the skull and inferior maxilla the most frequently. Carcinoma invades distant structures by way of the bloodvessels and sarcoma may be disseminated through the lymphatic channels with greater frequency than is the usual rule.

6. Malignant goitre causes death in at least 70 per cent. of cases.

Case I.—Woman, aged forty-eight years; married, mother of seven children; three miscarriages; has reached menopause; family history negative. Thyroid began to enlarge gradually sixteen years ago; during last four to five years the rapidity has increased. There is no pain but slight tenderness over the tumor. The patient suffers from dyspnœa and palpitation on exertion, and has had occasional nervous spells. On examination the tumor is the size of a large fist and lies mostly on the right side, extending laterally to the sternomastoid muscle, and is firmly adherent to surrounding structures. The goitre was removed under ether anæsthesia. Following operation there was some hoarseness, and the voice was reduced to a whisper; at the end of three weeks the patient was quite well. The tumor measures 10 x 8 x 5 cm., is irregular in shape, and has a smooth surface; the color is reddish gray. Microscopic diagnosis: adenocarcinoma. (Service of Dr. J. B. Deaver, op. spec. No. 606.)

Case II.—Woman, aged thirty-four years, married, no children. The thyroid enlargement was first noticed seventeen years ago. The growth was painless, freely movable, and about 11.5 cm. in diameter. For many years a small lump in the breast has existed; previous to admission this mass rapidly grew, but was painless; no retraction of skin. No glandular involvement. Breast amputated and thyroid extirpated after adhesions were freed.

The thyroid tumor is composed of glandular tissue; some acini contain colloid and appear normal; others show evidences of irregular shape and differences in the size of the lining of the cuboidal cells. These cells occur in many layers and in some instances fill the lumen of the acini. The stroma is dense and hyaline in appearance; contains some areas of calcification and thickening of the bloodvessel walls. Diagnosis: adenocarcinoma. (Service of Dr. J. B. Deaver, op. spec. No. 255.)

Case III.—Female, aged eighteen years, single. There is no history of either malignancy or goitre in the patient's family. About three years previous to admission the patient noticed a lump in the neck the size of a walnut; the growth has been slow, movable but painful. At present it is the size of a lemon and causes disturbance in deglutition. There are evidences of hyperthyroidization, nervousness, constant headache, palpitation, and dyspnœa. Under ether the entire left lobe, which was much enlarged and cystic, was removed.

The specimen consists of an oval mass of tissue 6 x 3 cm. The growth is firm and is surrounded by a fine fibrous capsule which strips off easily. On section the growth is rough and friable, and contains many small cavities about 1 cm. in diameter. Microscopic diagnosis: cystic goitre with beginning malignant degeneration, as is seen by the epithelial invasion of the stroma. (Service of Dr. J. B. Deaver, op. spec. No. 832.)

Case IV.—Man, aged sixty-six years, family and previous personal history are negative. A swelling on the right side of the neck has been present for twenty-five years; the growth has steadily increased until now it is the size of a cocoanut, with an irregular surface nodular and cystic in character. The trachea is pushed to the left with resulting dyspnœa; the skin is free, some dysphagia. The tumor is limited by the inferior maxilla above, the clavicle below, the middle line anteriorly and the scaleni muscles posteriorly. Operation: flap turned up, vessels tied; adhesions freed and tumor removed. There still remained a large, elongated, tumor-like formation occupying the location of the internal jugular vein and also a group of enlarged nodes at the root of the jaw. The elongated tumor was ligated and excised. It proved to be an enormous jugular vein filled with a degenerated clot. Respirations at this time became stertorous, cyanosis developed, and in spite of the usual remedies the patient died from shock. Partial autopsy performed; the tumor removed consisted of a cystic goitre in which an adenocarcinoma had developed. (Service of Dr. J. B. Deaver, op. spec. No. 1066.)

Case V.—Mrs. E., aged twenty-five years, mother of one child. Family and personal history negative. For the past four years the patient has had a goitre which because of its slow growth was not interfered with. During the past five months the tumor has rapidly increased in size, there has been loss of weight and strength, with dysphagia and an irritative cough. The entire left lobe was removed at operation, some slight difficulty arising in detaching the mass from the larynx. Following the operation the subjective symptoms were relieved, and the wound healed promptly; the patient is well eighteen months after extirpation of the growth.

Microscopically the tumor is composed of dense hyaline connective tissue containing much pigment. Into many cystic spaces which are present papillæ project. The latter are lined by a single layer of cylindrical epithelium, and its connective-tissue stalk is apparently the result of an hypertrophy of the glandular struma. In other portions the gland acini are of such irregularity and the cells sufficiently abnormal to suggest malignancy. Diagnosis: papillary cystadenocarcinoma. (From the service of Dr. Edward Martin, Surg. Path. No. 575.)

Case VI.—G. R., male, aged forty years; mother died of carcinoma of uterus. Patient gives no previous history of goitre, and seven months before admittance first noticed an enlargement in the thyroid region. The growth was rapid, and soon by pressure caused dyspnœa, dysphagia, cough, pain, and aphonia. There was also loss of weight, tachycardia, and exophthalmos. A tracheotomy for the relief of the dyspnœa was performed; the patient, however, died the following day. The autopsy revealed a tumor the size of an orange occupying

Fig. 1.—Case VII. Carcinoma of thyroid gland.

the left lobe. The growth was well encapsulated, firm, and on section presented a diffuse yellow and gray appearance. The mass exerted pressure on the bronchus so that its anterior wall was ulcerated for a distance of 5 cm. Metastasis was not found in the organs or bones. Microscopically considerable hemorrhage and necrosis were present, the stroma well developed and dense. The latter is infiltrated with irregular acini and strings of large epithelial cells, showing mitosis. Diagnosis: adenocarcinoma. (From the service of Dr. Martin, Surg. Path. No. 863.)

Case VII.—E. V., female; history of the case not known. The tumor occupies the right lobe of the thyroid, is about the size of a walnut, and well circumscribed. The growth is white in color but not of any considerable density. Microscopically evidences of previous struma are seen by the calcification and the overgrowth of fibrous tissue. Atypical glandular elements make up the greater part of the neoplasm;

a small amount of colloid is contained within the acini. Diagnosis: adenocarcinoma. (From the service of Dr. J. W. White, Path. Surg. No. 277.)

Case VIII.—M. R., female, aged forty-eight years; further record of the case has unfortunately been lost.

Microscopically the tumor is composed of a dense fibrous stroma containing areas of calcification. Into the cystic spaces which are present papillæ are seen. The connective tissue of the latter is delicate, the lining is composed of a single layer of cylindrical epithelium for the greater part, in some places the cells form several layers. Well-marked evidences are present in areas in which the acini are irregular, the epithelium of which is irregular in size and has broken through the basement membrane. Diagnosis: papillary cystadenocarcinoma. (From the service of Dr. Martin, Surg. Path. No. 322.)

Fig. 2.—Case IX. Spindle-cell sarcoma of (*a*) thyroid gland; (*b*) normal gland.

Case IX.—E. B., female, aged fifty years; admitted to University Hospital, service of Dr. C. H. Frazier, October 8, 1903. The mother and one sister of patient have goitres, but are alive and well.

In August, 1902, a swelling appeared on the right side of the neck, not painful and not increasing in size. In March, 1903, lymphatic nodes on right side became swollen during a few months and then remained stationary. No loss of weight. Upon admission the following note was made: On right side of neck, beginning 1 cm. below mastoid process, the chain of cervical lymphatics is much enlarged. Three masses may be palpated, loosely adherent and extending downward to the clavicle, not below it. To the inner side of the sternomastoid and occupying the position of the right thyroid lobe a globular swelling is found. Surface is smooth, consistence much harder than the normal thyroid, and rises and falls with deglutition. It is about the size of a small hen's egg and not attached to the glandular mass. Patient discharged October 10, 1903, untreated.

Re-admitted July 15, 1904. No change; operation July 18th. The tumor mass was found to involve the right lobe of the thyroid only. This was removed and the chain of affected lymph nodes, which extended down to and somewhat below the sternum, were removed without much difficulty. Hemorrhage was very free during the operation, owing to the presence of a great number of very much enlarged veins, some passing over and some traversing the goitre. Discharged August 11, 1904, with a small sinus.

Fig. 3.—Case IX. Spindle-cell sarcoma of the thyroid gland. Medium power drawing.

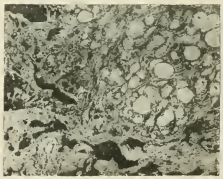

Fig. 4.—Case IX. Spindle-cell sarcoma of the thyroid gland. Low-power photomicrograph.

January 18, 1905. Patient has gained ten pounds. Has had some pain in neck during past three months. No evident recurrence.

July 4, 1905. Re-admitted with recurrence, some hoarseness and diarrhœa. Operation July 5, 1905. Four enlarged nodes were removed: two just above the clavicle and two over the lower portion of the lower triangle. No other involvement. Discharged July 14, 1905.

October 18, 1905. Re-admitted with recurrence. States that in August she fell and fractured left hip. Union of the fragments occurred. Operation October 23, 1905, and three nodes dissected out, one containing greenish pus. An

obstinate diarrhœa began shortly after this operation and continued until the death of the patient.

December 10, 1905. Liver noted as being enlarged.

February 11, 1906. Death three and one-half years from the onset of the swelling, one year and seven months after first operation.

The body was greatly emaciated, five feet two inches in height and weighing sixty-eight pounds. Rigor mortis slight, cadaveric lividity moderate; the skin of the entire body is somewhat bronzed. On the right side of the neck, extending from the median line toward the right ear and toward the median line of the lower jaw-bone, are a number of scars from previous operations. Just beneath the angle of the jaw is a small nodule, adherent to the skin, not ulcerated, about 1 cm. in diameter.

Fig. 5.—Case IX. Metastasis to liver from spindle-cell sarcoma of thyroid.

Gross Description of Growth.—Specimen consisted of a lobe of the thyroid, measuring 7 x 5 x 4 cm. in size, red in color, of irregular surface, and somewhat pyramidal in outline. Occupying most of the base of this tumor is a hard, yellowish fibrous tumor, not encapsulated from the thyroid tissue, although entirely within the gland.

Microscopic examination showed a spindle-cell sarcoma with but few bloodvessels and involving the interacinous connective tissue and trabeculæ of the glands. The vesicles seem to be surrounded and then destroyed by the advancing growth. Much of the tissue is composed of a hyaline-like connective tissue in which masses of the spindle sarcoma cells are present.

The lymph nodes are involved from the primary growth and contain no colloid material. In places it seems as though a direct metaplasia of the connective tissue of the node has occurred and the sarcoma occurred *in situ*. In other areas infiltration is evident. The nodes were hard and yellow in color.

The glands removed at the several operations were all identical, as were those removed at postmortem.

Autopsy was performed by Dr. Lavenson, twenty-four hours after death (848, 06, 15).

Anatomical Diagnosis. Sarcoma of thyroid with metastasis to liver; ulcerative colitis; chronic interstitial nephritis; brown atrophy of heart and liver atrophy of spleen; left-sided chronic adhesive pleurisy, emphysema and congestion of the lung.

The spleen weighed 48 grams, the left kidney 40 grams, and the right kidney 75 grams. The kidneys were the seat of interstitial change. The liver weighs 910 grams, is small, the left lobe participating more than the right in the decrease in size. The substance is soft and flabby; color, dark brown. Distributed over the surface are somewhat elevated, white or yellowish areas, well marginated, presenting a smooth surface and in most cases regular margins. In the neighborhood of the longitudinal fissure there is a mass about 3 cm.

Fig. 6.—Case IX. Metastasis to liver; spindle-cell sarcoma.

in diameter, having the same characteristics except that the edges were more irregular. On section similar areas varying from 0.5 to 1.5 cm. in diameter are found scattered throughout the organ. The liver tissue shows the normal markings to be somewhat indistinct and the surface of a dark-brown color. The other organs were normal with the exception of the large intestine, where particularly in the ascending and transverse portions the mucous membrane in areas is markedly congested.

The isthmus of the thyroid is apparently wanting, a portion of the left lobe is present and normal in appearance. In the region of the right lobe are four nodules, 1 to 2 cm. in diameter, firm, yellowish white in color and well defined from the surrounding tissues.

They have apparently produced no pressure symptoms, and the larynx and trachea are not diseased.

Microscopic examination of the nodes within the liver revealed a spindle-cell sarcoma, with very large cells and no colloid material present.

We are greatly indebted to Dr. J. B. Deaver and Dr. A. O. J. Kelly for the use of the specimens from the German Hospital, and to Dr. J. W. White, Dr. E. F. Martin and Dr. C. H. Frazier for the specimens from the University Hospital.

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B. J. C. D

A CASE OF PNEUMONIA IN A FOUR DAYS' OLD INFANT, DUE TO THE BACTERIUM MUCOSUS CAPSULATUS.

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(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

The case we are about to report occurred in an infant born in the Maternity of the University Hospital, in the service of Dr. B. C. Hirst, to whom we are indebted for the use of the clinical data. The child was born of apparently healthy parents, on December 12, 1905. Shortly after birth a temperature of 99.2 degrees was noted; this rose within forty-eight hours to 105. With the exception of two rises, one to 109, another 110, the temperature varied between 103 and 106 until the infant's death, four days after birth.

The autopsy was performed six hours after death, the following conditions being noted: marked cadaveric lividity; slight rigor mortis; in the abdominal cavity the organs showing pathological changes were the liver, stomach, and kidneys; in the liver, located just beneath the capsule, were numerous small hemorrhages, varying in diameter from two to six millimetres; these could also be found throughout the substance of the organ, but not in such large numbers; one quite large hemorrhage and several small ones were observed in the wall of the stomach; there was no free blood in the cavity of the organ; the kidneys revealed extensive uric acid infarction, which appears to have no connection with the other interesting features of this case. The only significance of these infarcts, in our present-day knowledge, is as an indication of the child having breathed.

Heart. Just beneath the visceral pericardium were to be seen many hemorrhagic foci, from 1 to 2 mm. in diameter.

Lungs. These viscera, though crepitant throughout most of their extent, give the impression of increased density, especially in the left lower lobe; just beneath the visceral pleuræ are about half-a-dozen areas of hemorrhage, varying in diameter from two to five millimetres; on section the lung presented some diffusely distributed, pinkish-gray prominences, approximately five millimetres in diameter; in the left lower lobe they tended to become confluent; there were, moreover, a few scattered hemorrhages in the tissues corresponding to those already described; bronchi and bronchioles presented nothing abnormal.

Histological Examination. Section of the affected portions of the lung showed a considerable number of the alveoli partially or wholly filled with an exudate, composed chiefly of epithelial cells and cell detritus, with a much smaller admixture of fibrin, leukocytes, and red blood cells; in one area the character of the exudate was almost purely hemorrhagic, the alveoli being filled with erythrocytes, with here and there a leukocyte; this hemorrhagic area extended peripherally to the pleura, was fairly well marginated, and showed no intensity of the process at the borders; the alveoli between those of exudation and hemorrhage were to a great extent free and partially distended.

Kidneys. The epithelial tissues of the cortex showed the changes characteristic of cloudy swelling to a moderate degree; the uric acid infarcts were very well seen, particularly in the pyramids

The liver showed a marked fatty infiltration.

The thymus body presented an unusually large number of epithelial nests; no areas of hemorrhage can be found.

The bacteriological report of this case has the following points of interest: the organisms were isolated from the lungs, heart, and blood of the child in pure culture, and from the liver, together with the colon bacillus; the bacterium was of high virulence, and was able in a remarkably short time to produce the same pathological lesions in guinea-pigs as in the child, leading to their death in 20 hours the first time, and in 24 hours at a second trial; the organism changed its biological reactions after cultivation and reculture from the dead animals. Rabbits were also susceptible.

As is well known, the group to which this culture belongs, *i. e.*, the B. mucosus capsulatus group, of which the Friedländer bacillus is the best known, is commonly associated with, and probably very frequently bears a pathogenic relation to, many acute diseases of the respiratory tract. Since the various reporters have differed so greatly in their descriptions of the individual strains we have not had a very satisfactory classification until 1904, when Perkins published his very good work on about thirty strains of this group. His results justified an arrangement of these cultures into three main groups, dependent upon their reactions with the carbohydrates: The first heading is the B. aerogenes group, in which are placed those strains which will ferment all sugars and some of the alcohols. The second division, the B. pneumonicum group, comprises those which break up these same compounds, with the exception of lactose. In this family come the original bacillus described by Friedländer—the B. rhinoscleromæ and the B. ozænæ. The third group, B. acidi lactici group, ferment all sugars but saccharose and include some infrequent strains beside the B. acidi lactici. Those organisms which do not break up lactose do not coagulate milk, which fact the author interprets as a corroboration of his classification.

If we attempt to classify the strain isolated by us according to these orders we find that at first it fell into the B. aerogenes group, but upon cultivation and recultivation it lost its power to ferment saccharose, and therefore is to be included with the B. acidi lactici division, which is evidently incorrect, because it fermented glycerin agar and rendered this medium acid, a property not possessed by this last-named family. The loss of ability to break up some of the sugars has been mentioned by a few authors in descriptions of this whole group, but Edwards (*Journal of Infectious Diseases*, vol. ii., No. 3) says that no organisms which have lost this power have been reported in relation to pathological processes. This loss of fermenting property has not yet been explained.

Despite this curious change of biological reaction we are convinced that the isolated organism belongs to the species described first by Pfeiffer. It is obviously not a Friedländer bacillus, because there was rapid acidification and coagulation of milk, and production of gas on lactose media. There was very much more gas on dextrose, saccharose, and mannite than on lactose media, a fact observed constantly by Perkins with the B. mucosus capsulatus, but not noticed by Strong. We therefore consider that its proper name is B. mucosus capsulatus, and its proper classification is with the B. aerogenes, as suggested by Perkins. Further refinements seem hardly necessary.

Morphological and Cultural Characteristics. This microorganism was a non-motile rod, losing the blue in Gram's stain, staining with the aniline dyes rather poorly, and showing a tendency to take the color more deeply at the poles. It varied in dimensions of length from one and a half to three times its width. Capsules were found in twenty-four-hour cultures in milk and in smears from the organs of the animals. These capsules were quite plump, and varied from a slight halo to a broad band, sometimes twice the thickness of the organism itself. More than one element was seldom found in a capsule. No spores or distinct polar bodies were noted.

Agar Slant. A smooth, flat, even, regular, glistening, slimy growth of a dull pearl-white color, showing no tendency to spread except into the condensation water. The edges were somewhat undulating. The stroke tended to become concave and the condensation water very slimy.

Agar Plates. The superficial colonies were round, discrete, convex, and entire, of a slimy consistency, and a dull pearl-gray color. They later became creamy and larger, but maintained their entire edge. They were found to be finely granular, with a dark centre becoming filmy toward the periphery, with entire edges, and of a general yellow-brown color when examined under the microscope. The deep colonies are large, yellow-white, and of whetstone shape. Microscopically they are round, elliptical, or of a whetstone shape, coarsely granular, and sometimes grumous.

Glycerin-agar slant culture partakes of the characteristics of the plain agar after the first twenty-four hours, but later there is so much gas that the growth is no longer peculiar.

Gelatin Stab. There is a filiform growth along the needle track, in which appear a few gas bubbles that do not increase after the third day. The growth on the surface is at first moderate in amount and of a pearl-white color. This later becomes more luxuriant, and at the end of seventy-two hours is distinctly convex, with a quite perceptible umbilication directly over the top of the needle puncture. There is never a true "nail growth." The surface colony flattens a little at the end of two weeks, but does not spread.

Gelatin Plates. The colonies are punctate, round, and grayish white macroscopically. Microscopically they are entire, even, round, or irregularly elliptical, finely granular, and of a light-yellow color. Later they become a creamy yellow, more homogeneous, and of a deeper brownish-yellow color,

Milk. After twenty-four hours the blue tint of litmus milk is lost and the medium is pink. There is also noticed a very viscid state of the lower half of the tube, which, at the end of another day, is firmly coagulated while the upper half is just beginning to clot. The whey is at top and of a pink color, while the clot has become entirely decolorized at the end of four days. There is little if any digestion of the coagulum.

Bouillon. A very abundant growth takes place in this medium, with the production of a stringy sediment and a thick pellicle, the latter not reappearing when once it is destroyed, its place being taken by a sort of scum.

Peptone-water. There is not very much cloudiness, and no pellicle. Indol reaction is positive, but feeble.

Potato. This medium gives a moist, irregular, creamy white, slimy, glistening growth along the stroke, with little tendency to spread except into the moisture at the bottom of the tube. The growth becomes a trifle watery at the end of six days, and a faint cheesy odor is noticeable. A few gas bubbles were noticed on the growth and many in the water.

Glucose-litmus Agar and Bouillon. This medium is changed from blue to pink and decolorized in twenty-four hours, with the production of gas; at the end of fourteen days the gas formula is $HCO_2 : 3$.

Lactose: Litmus Stab and Stroke. On the stroke the growth is pinkish and like on plain agar. The medium into which the stab was made was decolorized in three days, with the production of much gas.

Lactose: Neutral Red Agar. At first there is distinct increase in the red color, lasting three days, but this gradually gives way to a yellow tint, beginning at the bottom of the tube. There is naturally much gas. Decolorization is completed at the end of six days.

Lactose : Neutral Red Agar Bouillon. This medium in a test tube is decolorized in seven days, as is the case also in the bulb of the fermentation tube. At first by both methods the solution is redder, the vertical portion of the fermentation tube maintaining this tint continuously. There is a good growth in both sections of this tube. The gas formula is $HCO_2 : \frac{3}{2}$.

Mannite : Litmus Agar Stab and Stroke. The stab is completely fermented and decolorized in three days. The stroke, on the other hand, is not decolorized until the sixth day, and produces very little gas. The surface growth is pink. At the end of nine days the blue color of the medium returns, and it regains its original tint at the end of the second week. In the bouillon this sugar and litmus do not behave the same way. The test tube and fermentation tube become a purplish color after twenty-four hours, which they retain. There is formation of gas in the closed arm of the latter, which gives, at the expiration of fourteen days, a formula of $HCO_2 : \frac{1}{1}$.

There is a good growth on saccharose agar, but no gas production after the second sub-culture. The gas formula was not determined at the time this sugar was fermented.

Guinea-pigs were injected, on two occasions, with practically identical results. At the first injection, three days after the isolation, the pigs were given 1 c.c. of a twenty-four hour bouillon culture, and they died in twenty hours, exhibiting at autopsy congestion of the lungs, slight stringy exudate on the peritoneum, and a seropurulent fluid in the pleuræ. Cultures from all of the viscera gave pure cultures of the injected bacterium. After two weeks' cultivation pigs were again given 1 c.c. of a twenty-four-hour bouillon culture from both the original culture and from that obtained from the first pigs. They were found dead in twenty-four hours. Two pigs had received the injection directly into the lungs; while two had received it into the peritoneal cavity. Those which received the intrathoracic injection we will call pigs No. 1, and those which had the peritoneal infection, pigs No. 2. The pathological lesions were alike in both pigs of each set.

Autopsy of pigs No. 1 showed marked congestion of both lungs, liver, and kidneys; a serosanguineous fluid in the pleural and peritoneal cavities. Cultures were positive and pure. Pigs No. 2 also showed congestion of all the solid viscera, an area of congestion in the right lung, and a curious gelatinous appearance of the left upper lobe; there was also a purulent peritonitis. Cultures were as in the first pigs.

The lungs, liver, spleen, and kidneys were removed for section and comparison with those of the child. The sections were stained by the ordinary methods, and for bacteria.

In the lung of the child the bacteria could be demonstrated in the exudate in great numbers, especially where the blood infiltration is greatest. They are to be seen in the blood stream and in the interalveolar septa. There are some to be seen in the exudate, to be sure, but where the epithelial cells predominate they are conspicuously few in numbers. In the lungs of pigs No. 1 the picture of epithelial desquamation and proliferation, slight invasion of leukocytes, and absence of fibrin is the same as that shown by the baby's lung. In the pig there is a greater tendency to hemorrhagic infiltration than in the lung of the child. Here, as in the infant's lung, the bacteria are chiefly in the blood channels and extravasations, and in the alveolar walls. They are to be found in relatively greater numbers in the exudate itself than in the case of the child. There are some evidences of phagocytosis, which was not observed in the baby's lung. The lungs of pigs No. 2 gave the picture of a high degree of hemorrhagic extravasation, with some desquamation of the epithelium. Here the bacteria are conspicuously rare, and those present are in the blood channels. There is also some œdema.

The liver of the child shows a few bacteria in the blood channels, and one small clump was found in a bile duct. The No. 1 pigs' livers were the seat of a beginning cloudy swelling, and there were multitudes of organisms in vessels of all sorts, as well as in the parenchyma cells. Hemorrhagic infiltration was quite marked. The liver of the pigs which received the injection into the abdomen had the same pathological changes; there were, however, fewer organisms, only a pair of which were observed in the cells of the organ in looking over the two sections.

The spleens of the pigs are the same as that of the child, the only difference being the presence of organisms which are absent in the infant's spleen. The Malpighian bodies are unaffected.

The kidney of the child contained no demonstrable bacteria. That of the first pigs showed a moderate degree of parenchymatous degeneration, a congestion of the entire kidney, and an extravasation of the blood, especially into the pyramids and medullary rays. There was no blood in the capsule of Bowman. There were great clumps of organisms everywhere, including the loops of the glomerulus, and lying free in the capsule. They were to be seen in the renal epithelium and in the tubules. The kidney of pig No. 2 had suffered about the same pathological injuries, except that there is not so much bloody extravasation. The bacteria are present, but not in such large numbers. It is noticeable that the bacteria in this pig were usually in good-sized clumps, and were often situated within capillaries.

The foregoing facts seem to indicate that this organism is the cause of the infant's illness, and that it has set up an infection, which, while in no manner like that of its congener the Friedländer bacillus, is quite virulent and of a hemor-

rhagic type, suggestive of the possibility of the attainment by this germ of a high grade of virulence.

The isolation in pure culture of the organism and the absence of other bacteria from this case seem to stamp as erroneous the view that this group of micro-organisms is only secondarily involved in the causation of pneumonia. But it must not be forgotten that we are here dealing with a general infection which was clinically more manifest in regard to the lungs. The gross appearance of this lung was not that of the gelatinous Friedländer pneumonia, but it is by no means an uncommon occurrence to find in children a lobular pneumonia, caused by an organism which usually produces the lobar type in adults. Hemorrhagic conditions of the lungs may be found in many severe infections in infants, but the consistent actions of the isolated bacterium give us ground to ascribe to it a specific activity here.

Some other pulmonic infections by this group have been observed by the writers, which will be the subject of a later communication.

HYSTERIA SIMULATING BRAIN TUMOR, WITH A REPORT OF TWO CASES.[1]

By T. H. Weisenburg, M.D.,
Instructor in Nervous Diseases and Neuropathology in the University of Pennsylvania.

(From the Department of Neurology, University of Pennsylvania.)

It is well known that hysteria may resemble in its symptomatology almost any organic nervous disease, and that a differential diagnosis is at times most difficult. This is especially so if there really exists some organic disease, and the hysterical symptoms are superadded.

While our conception of the nature of hysteria is by no means clear, it is probable that the disease is of cerebral origin and depends upon a temporary perversion of function of the cortical or basal centres. By no other means can we explain such symptoms as hemiplegia, monoplegia, disturbances of sensation, of vision, and so forth.

It must also be remembered that in almost every organic nervous disease, indeed it may be said that in any disease of any organ or of any portion of the body, some neurasthenic or hysterical symptom may be found. Every physician encounters it daily in his practice and it is the recognition, treatment, and the cure of this that makes the successful physician.

It is a question, at times, whether it is more difficult to recognize hysterical symptoms from organic or the reverse. No better illustrations of this can be found than in the disease, multiple sclerosis. Brain tumors offer at times the same difficulty, cases being recorded in which hysteria was diagnosticated, whereas at necropsy a brain tumor was found, and others, in which the so-called organic symptoms were really hysterical. If the latter error is committed it may lead to serious results, for a needless surgical operation may be performed for brain tumor. The writer has recently had under his observation such a case, and the record of a similar case is given, for the notes of which he is indebted to Dr. Wm. G. Spiller.

[1] Read before the Medical Society of the State of Pennsylvania, held at Scranton, September 26 and 28, 1905.

Case I.—A woman, thirty-two years of age, was sent to me by Dr. John T. Krall, of Philadelphia. She was a weaver, her occupation necessitating perfect sight, as she was required to weave sixty threads to the inch. The patient had always been healthy, and, previous to her present trouble, had a slight attack of grip, but this did not stop her from working. On a Sunday morning she woke up at three o'clock and vomited, and again at six. She had a little headache, but otherwise felt well. After a short nap in the afternoon she awoke to find herself completely blind, in which condition she remained for three months before she came under our observation.

Dr. Krall reported: O. D., cornea clear, pupil dilated (no drops) 7 mm., round; media clear, the nerve outline is distinct; atrophic cupping, white atrophy; vessels small; macular region shows disturbance of pigment. V = 10 cm. 60.

O. S., V = 10 cm. 50. General appearance similar to O. D., except a small regular round patch of choroiditis in the inferior and temporal side. The reactions to light, accommodation and convergence were sluggish in both eyes.

When examined by me, except for the loss of vision, she did not complain of headache, nausea, or vomiting. She was however, irritable, would become easily excited, and complained of feeling "weak" all over the body. Station and gait with eyes open or shut were normal, but she had a tendency to stagger a little with her eyes shut. She could wrinkle her brows evenly on both sides, but on showing her teeth, either on one side or bilaterally, fibrillary tremors were noticed in the facial distribution, with some weakness. There was no other involvement of the cranial nerves. Hearing was acute. Taste and smell were not disturbed. Power was diminished in both upper and lower limbs, a little more on the left. The tendon reflexes were prompter

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than normal, a little more so on the right side. Sensation was normal for all forms. Some ataxia was present in both upper limbs, and about equally so.

Associated ocular movements were well performed downward and to the right, but associated movements to the left and upward were limited, especially in looking upward, where every attempt would be accompanied by a wrinkling of the brow. No hysterical stigmata were found at this time.

Because of the paresis of associated ocular movement to the left and upward, the apparent weakness of either seventh nerve and the optic atrophy, a tumor near the oculomotor nucleus was thought of. The symptoms were, however, by no means clear, and the diagnosis of hysteria was held in reserve.

A few days afterward examination denoted entire absence of paralysis of associated ocular movement either laterally or upward, and a further examination by Dr. Krall showed that vision could be improved considerably by suggestion. Although the patient stated that she could not see, objects purposely placed in her way would be properly avoided, and she would occasionally recognize fine type, while at other times this could not be recognized.

The apparent atrophic cupping of the optic disks may have been physiological, although their appearance was typical of such degeneration. The patient improved considerably under treatment, but passed out of our care, so it is impossible for us to say how far she finally improved.

Case II.—A single girl of twenty years, whose family history was negative. The patient had always been nervous and easily offended, but had otherwise been well, except for occipital headaches, which she had two or three times weekly since her twelfth year. A year before she came under observation she had her appendix removed, since which time she has complained of severe headache, nausea, vomiting, and vertigo. These symptoms became exaggerated during the six weeks before her admission to the University Hospital, and she also then first showed some inco-ordination in walking, which later developed into complete inability to walk, and she was confined to her bed. She also complained at this time of diplopia, and her physicians naturally thought of brain tumor. Dr. Spiller was called in consultation by Dr. Applebach, and she was admitted to the University Hospital.

At this time the patient complained of headache of a sharp character, which she described as resembling the noise made by the passing of a train of cars. Nausea, vertigo, and vomiting were also complained of. She was unable to stand without support, and would stagger on attempting to walk, but it was doubtful whether she would have fallen. During the examination the patient frequently jerked all over the body, and would throw herself around the bed. The eye examination showed a hippus on either side. The visual fields were normal. The patient later complained of temporary right monocular diplopia. The optic disks, except for a slight congestion of the vessels, were normal. The cranial nerves were normal. The limbs were a little weak, but resistance to passive movements could be increased on encouragement. The tendon reflexes of both upper and lower limbs were exaggerated. There was no ankle clonus or Babinski response. There was no atrophy anywhere. Sensation for touch was normal all over the body, but pain sensation was felt more acutely on the left side. Later touch sensation was more acute on the right and pain on the left. Hearing was acute. The sense of smell was lost and taste impaired. The right nostril was more sensitive than the left. The pharyngeal and conjunctival reflexes were preserved. She had marked inguinal and inframammary tenderness on the left, but not on the right.

Because of the manifest exaggeration of the symptoms as in walking, the presence of such hysterical stigmata as inframammary and inguinal tenderness, loss of sense of smell and impairment of taste, disturbance of sensation and the absence of organic symptoms, the diagnosis of hysteria was made. Suggestive treatment soon effected a cure.

Later the patient admitted that she had for the past year frequently discussed the symptomatology of brain tumor with a girl friend who did have such a neoplasm, and that gradually she began to complain of the same symptoms. It was not until an *x*-ray picture conclusively proved to her that such was not the case that she accepted the fact that she had no brain tumor.

These two cases illustrate well the difficulties encountered in diagnosticating brain tumor. At the first examination in each brain tumor was thought of, although a suspicion was aroused because of the bearing of the patients and the rather unusual symptomatology, as in the first case. The second case had the typical symptoms of brain tumor, and only careful observation permitted a correct diagnosis.

TYPHOID FEVER—ACCIDENTAL INFECTION WITH GAS BACILLUS OR BACILLUS OF MALIGNANT ŒDEMA—DEATH WITH SYMPTOMS OF INTRATHORACIC IRRITATION. REMARKS UPON GIVING OF HYPODERMOCLYSIS.

By Norman B. Gwyn, M.D.,
Instructor in Medicine, University of Pennsylvania.

The following case may be of interest owing to the fatal accident occurring as a result of a very well-known and more or less simple procedure. I am indebted to Dr. Musser for permission to report it.

On November 11, 1904, W. A., aged thirty years, who had been ill for two weeks, complaining of lassitude and headache, consulted Dr. Musser. Widal reaction was positive on November 16th. Spots appeared in great numbers on the abdomen. Temperature running between 104° and 105°. Great distention of abdomen. Spleen area and liver dulness present. Quite delirious at this date. Pulse, 108 to 120. On November 18th, pulse tension low and rate higher; hypodermoclysis ordered, and repeated every six hours. First, under right breast; second, under left breast; third, into right thigh. Pulse reacted. All areas remained sore for many hours. Hypodermoclysis into right breast and left thigh at midnight, on November 19th. At 3 A.M. on November 20th there was marked cyanosis of back and poor low-tension pulse. Very delirious. Distention and diarrhœa very persistent. Some soreness over left breast and swelling over clavicle and shoulder; during the night of November 19th respiration began to rise, rapidly reaching 52 per minute, and remained high. No signs of pulmonary consolidation or œdema, the breathing suggesting more diaphragm irritation; rapidity persisted all day November 20th without influencing pulse to any appreciable degree. Abdominal distention lessened after using turpentine and milk of asafœtida, particularly in epigastrium, wind being brought up by way of the mouth. Still delirious; some redness over left chest and distinct swelling of pectoralis major. At 10.20 A. M. on November 21st pulse began to fail rapidly, running up to 120, and becoming weak and threadly. Distinct crepitations throughout tissues of left breast. Lungs clear. Spleen dulness present; liver dulness present. Lavage (600 c.c. fluid removed from stomach), some relief. Respiration continued rapid, but patient was evidently delirious. For rest of day pulse ran from 140 to 180, at times not being felt at wrist. Heart sounds remained fairly strong; no evidence of pneumothorax; sounds distant, but the tissues over left base and axilla were thickened and œdematous; some dulness more or less marked at base. The left breast is livid, purplish; distinct amount of air or gas in tissues, and feeling as if parts of tissue were liquefied. Redness and lividity extend over clavicles. Pulse remained unaltered from 4.30 P. M. until 4.30 A.M. on November 22d. Patient died at 6 A.M. Up to two hours antemortem patient was remarkably clear, being, in fact, more conscious six hours antemortem than eighteen hours antemortem. A second attempt, eight hours antemortem, to perform lavage was resisted violently, the patient seeming stronger and more active than eighteen hours before. A convergent strabismus developed a few hours before death; no cervical rigidity. Air (gas) could be manipulated from the soft breast tissues out through the needle-hole of the hypodermoclysis. An intense odor of H_2S was perceivable on doing this, and a black fluid could be expressed. This fluid, preserved and sterilized at once by alcohol, shows no blood cells but a granular débris in which can be demonstrated large bacilli, resembling in shape the bacillus aerogenes capsulatus; no spore-bearing forms could be seen. No culture media being on hand, this step was taken to rule out development of contaminating organisms, more particularly the hay bacillus, the morphology of which is practically identical.

The most interesting clinical conditions in the case were: first, the sudden development of rapid heart action and rapid respiration, the continuance of the same for so many hours, and, finally, the disappearance of the toxic symptoms of typhoid, while the local symptoms of the tissue infection progressed.

We are all familiar with the increasing rapidity of pulse and respiration of fatal toxæmias; in this case, however, the sudden onset and character of the symptoms were more suggestive of a pleuropulmonary or cardiac accident (such as pneumothorax). The remarkable clearness of intellect and very apparent gain in strength shown by the patient in the last twelve hours did not indicate a progressive intoxication.

When one is familiar with the local effects of bacillus maligni œdematis or of the gas bacillus a reason for the symptoms noted is apparent; the destructive power of these organisms is intense and gas formed in the precordial area would have but little difficulty in finding its way into the pericardium or into the pleuropericardial tissues. Only a very few bubbles of gas would be required in these regions to give rise to most marked symptoms; and we believe it seems more likely that direct irritation of the heart and pleura was taking place than that the symptoms were due to the toxæmia of the added infection,

With regard to infections by these organisms, it may be

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generally said that their beginning is usually in some area of necrotic or damaged tissues, hence the report of so many cases in mangling of extremities, in extensive burns or lacerations, in the uterus after labor, etc. That more instances are not seen is due to the fact that the bacillus is a rigid anaerobe and must get deep enough into the tissues to be away from the air before beginning to flourish. Under certain conditions, not well understood, spores are formed; and it is in such form that the organism is probably introduced into the body: the resistance of spores to ordinary methods of sterilization is too well known to need further comment, and the spores of this bacillus are no exception to the rule. Once deposited in a favorable spot growth is rapid, and in tissues severely damaged, liquefaction and gas-production (the characteristic qualities of these organisms) is rapid, being apparent in from three to four hours; under less favorable circumstances from twelve to twenty-four hours or more may elapse before enough gas has been formed to attract attention. In an open wound detection and recognition may be easy; in concealed spots or subcutaneous infection extensive damage may have been done before the nature of the trouble has been suspected.

In our case the long needle used and the bruising of the tissue by the introduced fluid gave to the organism the damaged tissue necessary for its growth. The depth of the infected area, concealing its nature, did not allow us to make a diagnosis until too late. It is more than possible that free incision of the breast region might have relieved the condition, but the difficulty of completely removing these infections is well known.

The question as to the identity of the micro-organism causing these infections is an interesting one; formerly, previous to ten years ago, all these emphysematous gangrenes and gaseous destruction of tissues were ascribed to the bacillus maligni œdematis. The discovery of another gas producer at this time has shown us that this latter, the bacillus aerogenes capsulatus, is the organism most frequently found; its relatively rare spore-formation and absence of motility differentiate it with difficulty from the bacillus maligni œdematis. I do not feel that microscopic appearance alone allows us to attempt to distinguish in our case. However, the general opinion now held by those of us who have had opportunities to study cases of emphysematous gangrene is that the so-called gas-bacillus is by far the more commonly found organism in these conditions; and the now numerous reports of infection by this bacillus, both antemortem and postmortem, and comparative rarity of reports of infections by the bacillus maligni œdematis show that many of the older records of bacterial findings in emphysematous gangrene must receive correction.

With regard to hypodermoclysis a few words may be said. We probably have all come to regard the procedure as simple, and one that is rarely followed by ill effects; in fact, much more trouble is experienced with small hypodermic punctures of certain drugs. In the past, in emergencies, little or no care has been taken in the line of sterilization in many instances; but such a happening as we have described, even where all precautions were taken, shows the need of absolute cleanliness, and the recognition of the possibility of serious after effects. I have once before seen a patient treated to a daily chill and temperature through imperfectly sterilized gelatin used hypodermically in the treatment of aneurism; the hay bacillus flourishing abundantly in the solution. My own idea is that "normal salt solution" should be carefully prepared in bulk (the concentrated solutions give chance of contamination in the corking and uncorking of the small bottles), and given the pasteurizing treatment; that is successive sterilizations in an autoclave or steam sterlizer. This we insist upon for our bacterial media, and know that it will spoil if not so treated; how much more careful should we be of a pint or quart of fluid to be put under a patient's skin.

The concentrated solutions on the market give extra chances of contamination in the corking and uncorking of the vials; one of these preparations was used in our case.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN

THE SIGNIFICANCE OF THE "FIBROGLIA" FIBRILS: AN EMBRYOLOGICAL STUDY.

By Arthur F. Coca, A.M., M.D.,
Formerly Demonstrator of Pathology, University of Pennsylvania.

In May, 1903, Mallory announced the discovery of a fourth variety of fibril produced by connective tissue cells, to which he gave the name "fibroglia," after the analogy of the neuroglia and myoglia fibrils. The work was published in December of the same year.[4]

Several methods of demonstrating the fibrils were given, the most important of which had been originated by himself, viz., the phosphotungstic acid-hæmatoxylin stain, and the aniline-blue stain—originally designed for the differentiation of white fibrous connective tissue fibres.

As to their situation, Mallory says: "These fibrils as a rule are not very common in normal tissues, except possibly in one situation to be spoken of later, and have to be hunted for with an oil-immersion lens. I have made no particular search for them, but have noted them, among other places, in the dense fibrous tissue of the breast, the corium, and the pia of the spinal cord. They usually occur singly or in small clumps. In the embryo they make their appearance in certain regions where the connective tissue is dense, as around cartilage, at a comparatively early stage, that is, at least as early as the time when the smooth muscle cells are acquiring their differentially staining fibrils. The most interesting field for their study is in inflammatory tissue of all sorts, more especially where it is growing rapidly, as, for example, in granulation tissue, in the stroma of carcinomata (especially the medullary carcinomata of the breast), and in other tumors in which connective tissue plays an important part. In other words, these cell fibrils follow closely the fate of the connective tissue cells: they are numerous and prominent when the cells are abundant, active, and proliferating; they are hard to find when the cells are few in number and in an inactive state."

Of their relation to the cells he says: "They bear the same relation to the cell protoplasm that neuroglia fibrils do; that is, they touch or run through the outer surface of the protoplasm and continue indefinitely in two directions; one end does not start in the cell. The fibrils from one cell apparently run to other cells, so that they are all more or less connected together."

Concerning their significance he says, "If the fibrils existed only in connective tissue it might be thought, in consequence of their extending apparently from cell to cell, that they had something to do with the relation of the cells to each other, but their presence in large numbers in the true basement membrane of various glands and beneath the endothelium of bloodvessels is against this view, and favors the idea that they have elastic or contractile properties."

The present study began in the McManes laboratory of pathology of the University of Pennsylvania, has been pursued for the greater part in the clinical laboratory of the Luisenheilanstalt at Heidelberg, for which latter privilege the writer is deeply indebted to the director of the institution, Professor Vierordt.

Technique. Chicken embryos were used exclusively. The eggs were opened under 85 per cent. salt solution at 39° C.; the embryos, after cutting of the vitelline membrane outside the limit of the blood circulation, were floated upon the convex surface of a watch crystal, on which upon removal from the solution they were directly treated with Zenker's fluid by means of a medicine dropper. By this procedure the yolk sac was fixed in a perfectly extended position and never became wrinkled or folded. After the superficial layers had become hardened—in a few minutes—the embryos were floated off into a dish of Zenker's fluid, in which they were left for from four to twelve hours, depending upon their size.

The subsequent treatment was quite regular. Serial paraffin sections were cut at 4 microns, usually at right angles to the long axis of the embryo, in a few cases parallel with that axis.

Of the staining methods recommended by Mallory the phosphotungstic acid-hæmatoxylin procedure gave, in the writer's hands, the clearest and most reliable preparations. The aniline-blue stain was also routinely used. Beside these methods another, hit upon in the course of the study, has proved useful. Its chief advantage lies in the sharp contrast—red against blue—between the fibrils and the cell protoplasm.

It is as follows:

1. Zenker's fixation; paraffin sections.

2. Concentrated aqueous solution of magentaroth(Grübler) twenty minutes in paraffin oven at 54° to 56° C.

3. Rinse in water.

4. Stain five to ten minutes in the following, using it cold: indigo-carmine (Grübler), 0.75 gram; saturated aqueous solution of picric acid, 100 c.c.; distilled water, 100 c.c.

5. Pass *rapidly* through 95 per cent. and absolute alcohol (using drop bottles) to xylol and balsam. Myoglia, fibroglia, fibrin and nuclei of cells, red. Connective tissue fibres blue. Protoplasm of cells, including epithelial cells and muscle fibres, yellowish green to greenish blue. Protoplasmic fibrils of the epidermis as well as neuroglia unstained. In making the phosphotungstic acid-hæmatoxylin the writer has used potassium permanganate as an oxidizing agent, and has found that by using the water at 60° C. and leaving the newly made stain in the paraffin oven at 56° C. for twelve hours the solution will stain at once as intensely as that which has been made in the cold and has stood for a year. The precipitate which forms by this treatment should be removed by filtration; it does not recur.

The principal object in this study has been to see what light, if any, can be thrown upon the function of the "fibroglia" fibrils by noting the time and site of their earliest appearance in the embryo. The present communication will, therefore, be naturally divided into two parts: first, a statement of the histological findings; and secondly, the possible interpretation.

Histological Findings. In an embryo of thirty-eight hours' incubation a few segmented fibres, staining by all the methods given by Mallory as well as by magenta, appear in the syncytial mass of cells which constitute the body of the heart wall. These fibres have been already described by Heidenhain and represent the earliest contractile element (Fig.1). With this exception no trace of any fibrillar structure has been found in the embryo up to and including this stage.

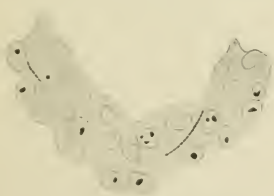

Fig. 1.—Contractile fibrils of heart wall; thirty-eight hours. (Camera lucida drawing; oc. No. 4, 2 mm. oil immers. lens, Zeiss.)

Between the thirty-eighth and forty-eighth hour no preparations have been made.

In an embryo of forty-eight hours, in addition to the segmented fibres of the heart wall, which are greatly increased in numbers, are found numerous unsegmented fibres possessing all the tinctorial affinities of the fibroglia fibrils. These are found in but one situation, namely, in the yolk sac.

The situation of the fibrils in the yolk sac is indicated in Fig. 2, which represents the membrane near its outer edge. The fibres are quite numerous in all parts of the sac, particularly near the body of the embryo; they extend also an appreciable distance beyond the limit of the blood circulation. In no place here do they show any intimate relationship with the bloodvessels.

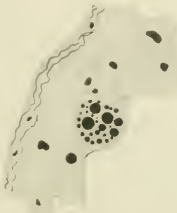

Fig. 2.—Fibrils of the yolk sac, near outer border, third day. (Camera lucida drawing; oc. No. 4, 2 mm. oil immers. lens, Zeiss.)

In an embryo of three days' incubation, in addition to the fibres already mentioned, segmented fibres, identical with those of the heart wall, appear in the "muscle-plate." The sheath of the chorda dorsalis at this time is clearly marked. In the earlier stages no element of the embryo has responded to the aniline blue of Mallory's connective tissue stain; now, however, this color is retained by the chorda-sheath diffusely just as it is in cartilage. Encircling the chorda and forming the inner boundary of the sheath are found unsegmented fibres which respond to all the stains for fibroglia (Fig. 3).

The bloodvessels of this embryonal stage, including the aortæ at their exit from the heart, show no trace of the subendothelial fibres of adult vessels.

On the fifth day white fibrous connective tissue fibrils make their first appearance in the embryo in the yolk sac. They are easily demonstrated at this time by the use of Mallory's connective tissue stain. Fibroglia fibrils are increased in the yolk sac and the fibrils of the chorda-sheath are still present.

On about the sixth day myoglia fibrils are demonstrable for the first time in the muscular coat of the œsophagus and in lesser quantity in the media of the aortæ.

On the seventh day cartilage has already made its appearance in the tissue about the chorda dorsalis, but does not completely surround the latter. The fibres of the sheath have now disappeared with the exception of traces in that part which lies between the chorda and the spinal cord, where cartilage is not yet laid down.

At this stage no fibrils can be found in the connective tissue of the body wall.

The earliest instance of the formation of fibroglia in the last-mentioned situation was found in an embryo of nine days, when a moderate number of cells were found in which a single fibre, beginning at a point near the nucleus, extended through a protoplasmic process, as shown in Fig. 4. In no case could the fibre be traced to another cell nor could it be found passing a nucleus in the manner described by Mallory in granulation tissue.

Fig. 3.—Portion of chorda dorsalis, showing fibrils of the sheath; fourth day chick. (Camera lucida drawing; oc. No. 4, 2 mm. oil immers. lens, Zeiss.)

Fig. 4.—Cell from body wall of chick embryo, nine days; fibroglia fibril in protoplasmic process. (Camera lucida drawing; oc. No. 4, 2 mm. oil immers. lens, Zeiss.)

Interpretation. The first question to suggest itself upon a review of the above-mentioned facts is whether all the fibres described as responding positively to all the staining processes known to be applicable to "fibroglia"—excluding, of course, those of muscular origin—are in fact "fibroglia" fibrils, and we may preface our argument upon the question by an analysis of the processes referred to. Assuming in all cases fixation of the tissue by Zenker's fluid: Fibroglia and myoglia are stained by (1) phosphotungstic acid hæmatoxylin; (2) the special acid-fuchsin stains, including Mallory's connective tissue stain; (3) magenta.

Fibrils of surface epithelium are stained only by phosphotungstic acid-hæmatoxylin.

Neuroglia fibrils are stained only by the acid-fuchsin stains, including the connective tissue stain of Mallory.

The early fibrils of the yolk sac can be pretty safely considered a product of mesoblastic cells that correspond physiologically with the connective tissue cells of the adult, for on the one hand a reference to the above analysis will suffice to exclude the ectoderm, while on the other the entoderm is not known to produce such fibrils. Studnicka,[7] it is true, has described a fibrillar constitution of the chorda cells of the lower fishes, reptiles, and even higher animals, but such fibrils are certainly not demonstrable by phosphotungstic acid-hæmatoxylin.

Regarding the fibrils of the chorda-sheath, the only argument favoring a mesoblastic origin is a weak one, namely: that we find no other cells of entodermic origin producing such fibrils, whereas the connective tissue cells, taking their origin in the primitive segments which lie in the immediate vicinity of the neural canal and chorda, are known to do so.

It may be said however, in circumstantial support of the view, that the first act of the original connective tissue cells is to surround the chorda by means of their power of amœboid movement, before which event the fibrils of the sheath have not been formed.

The analogy of the corresponding structure in the lower fishes may also be used in this connection. Von Ebner[8] has shown that the chorda-sheath of the lower fishes is in large part composed of a fibrous structure which in optical, chemical, and staining properties is identical with "collagen" or white fibrous connective tissue fibres, and which yields gelatin. The connective origin of the structure in these animals will scarcely be denied.

The function performed by the fibrils of both the yolk-sac and chorda-sheath is obviously analogous to that of the white fibres of the connective tissue in the adult. In the former instance it fortifies the membrane against the tension brought to bear upon it as the embryo increases in size, bearing the burden alone till the fifth day, when its ultimate successor—the white fibre—comes to its assistance; in the latter it takes part in the general function of the chorda, that of support to the delicate body of the embryo. And here again the analogy of the chorda-sheath of the lower fishes offers significant evidence in favor of the view stated above. Finally, the disappearance of the fibrils upon the appearance of cartilage indicates not only the function ascribed to them but their essentially transitory nature.

The appearance of fibroglia, as the first fibrous constituent of the connective tissue of the body wall, establishes its function as the physiological representative in the embryo of the white fibrous connective tissue fibrils.

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It may be added that this relationship is further emphasized by a study of granulation tissue, in which also the transitory fibroglia precedes the permanent elements, supplanting fibrin as a support to the new tissue.

No positive evidence, pointing to an "elastic or contractile" function on the part of fibroglia, can be deduced from the foregoing study, while, on the other hand, the absence of the fibrils in the vascular system for a considerable time after their first appearance in other situations may be considered negative evidence against such a view. Another significant fact bearing upon the point is one already noted by Mallory, that the subendothelial fibrils run not in a circular direction but longitudinally.

The difficulties attending the interpretation of the fibrils found in relation to the renal tubules, the coil glands of the skin, and the ducts and glands of the breast remain, so far as this research has gone, still unsolved; but those difficulties will hardly be used against the deductions reached by the study, since the anatomical source as well as the physiological function of those fibrils is still in question.

The histogenesis of fibroglia seems to be pretty clearly shown, namely, that it is an internal product of the cell protoplasm, and that, originally at least, it extends from cell to cell through the protoplasmic processes.

Conclusion. Fibroglia represents the embryological forerunner of the white fibre of adult connective tissue, exercising the functions of that tissue rather than those of elasticity or contraction.

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EXPERIMENTAL ARTERIOSCLEROSIS BY ADRENALIN INOCULATIONS AND THE EFFECT OF POTASSIUM IODIDE.[1]

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and

P. S. Stout, M.D.

(From the Pathological Laboratory of the University of Pennsylvania.)

It appears conclusive that arteriosclerosis may be produced in rabbits by the intravenous inoculations of adrenalin. Owing to the hypertension of the blood circulatory apparatus incident to these inoculations it occurred to one of the writers to attempt the prevention of the arterial disease by employing a drug which reduces blood pressure and assists in the absorption of exudates, etc. Potassium iodide was chosen. It has already been shown by Prevost, Binet and others that the iodide in large doses produces diminished vascular tension, and is efficacious in overcoming the spasmodic condition of the sclerosed vessels.

The experimental work is embodied in two series of animals. The inoculations were commenced on July 11, 1905. The adrenalin was injected into the posterior auricular vein, while the potassium iodide was given intravenously, subcutaneously, and by the stomach tube. The first series was composed of five rabbits, two controls receiving adrenalin alone and the remainder both adrenalin and potassium iodide, one of which received the latter by a stomach tube. The drugs were administered every other day. Adrenalin 0.1 c.c. was the initial dose and was gradually increased to 0.5 c.c. The maximum amount received by any rabbit was 6.4 c.c. The initial dose of potassium iodide was 0.012 g. and was increased every time by a similar amount until 0.23 gm. was given. Maximum amount received was 2.43 gm. The results as noted by the autopsies were negative.

The second series was composed of six rabbits. All received adrenalin. Nos. 1 and 2 were chosen as controls, with adrenalin alone; Nos. 3 and 4 were to be given inoculations of potassium iodide immediately following adrenalin; Nos. 5 and 6 were to receive no iodide until Nos. 1 and 2 had died with manifestations of arterial disease. The object in the cases of 3 and 4 was to overcome directly the effects of the adrenalin; 5 and 6 were offered as examples to ascertain whether or not the iodide had any effect after disease of the vessels had appeared.

Inoculations were commenced February 24, 1906. The veins of the ear were chosen as a seat of the inoculations. Warm test-tubes were employed to overcome the marked vasoconstriction. Throughout the experiments Parke, Davis & Co.'s adrenalin chloride 1:1000 and a solu-

[1] Presented at the Pathological Society, May 10, 1906.

tion of potassium iodide, a grain to a minim, were employed. The inoculations were given twice weekly. The initial dose of adrenalin was 0.1 c.c., and the amount was increased 0.1 c.c. every second time. Potassium iodide was started in 0.012 gm. doses and was increased in a similar manner to the adrenalin. No. 1 was emaciated when the inoculations were begun and was the first to succumb. It died March 29, after having received ten inoculations of adrenalin or 3.1 c.c. No. 2 died April 10, after having received thirteen inoculations of adrenalin or 5.5 c.c. No. 3 died April 6. The same number (thirteen) of inoculations as No. 2 was given, *i. e.*, adrenalin 5.5 c.c., and in addition 0.73 gm. potassium iodide. No. 4 died April 7, with a total of thirteen inoculations, and having received precisely the same amount of adrenalin and iodide as did No. 3. No. 5 was killed May 1, after having received twenty-two inoculations of adrenalin or 18.1 c.c. Following the deaths of Nos. 1 and 2, the iodide was commenced with a dose of 0.024 gm., and rapidly increased until a total of 1.5 gm. of nine inoculations was reached. No. 6 was killed May 1, and received the same treatment as No. 5.

All the rabbits had received a mixed diet of oats and cabbage and had maintained a good weight, barring No. 1. Ophthalmoscopic examinations were made, with negative results.

Postmortem Results. No. 1 showed a small atheromatous plaque in the arch of the aorta, otherwise the vessels were normal. No. 2 likewise showed a rather large plaque in the aortic arch. *In Nos. 3 and 4 the aortas were free of sclerosis.* No. 5 showed extensive disease from the aortic cusps to the bifurcation of the aorta. No. 6 showed several small plaques along the thoracic aorta.

Histological examination of the aortas of Nos. 3 and 4 confirms the report of the gross examination.

Koranyi has very recently reported a series of animals treated with adrenalin and potassium iodide, with results similar to ours ("Ueber die Wirkung des Jods auf die durch Adrenalin erzeugte Arterionekrose," *Deutsch. med. Wochen.*, April 26, 1906, pp. 679-680).

Examinations of the blood were made before and after the inoculations by Messrs. O. H. P. Pepper and J. H. Austin, of the University of Pennsylvania. Their report will follow in the fall. To them and Mr. A. N. Creadick we wish to express our thanks for their kindly assistance.

We offer but a small number of animals to show the results of the work, and this serves merely as a preliminary report. However, we state tentatively that potassium iodide may be effectual in preventing the development of arteriosclerosis after adrenalin inoculations. It seems probable that the iodide has no effect in its otherwise absorptive properties, after the arteriosclerosis has once appeared. Histological examination of all the tissues of Series II. will be made. A continuance of the work is contemplated by studying a much larger number of animals, with comparative studies. A complete report will follow in the very near future.

THE TREATMENT OF THE ADVANCED FORMS OF PROLAPSE OF THE UTERUS AND VAGINA.[1]

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The anatomy and pathology of the injuries of the pelvic organs and their supports resulting from childbirth, their sequelæ, and plastic surgery for their repair have received comparatively little noteworthy attention during recent years. It may be said, and quite truly, that this seeming want of interest is due for the most part to the long since published and accepted very scientific anatomical studies of these injuries and their sequelæ by Thomas Addis Emmet, and, based upon this study, the invention of the Emmet and other operations. Such operations devised for the repair and amputation of the cervix uteri, and those for relaxation of the perineum and anterior vaginal wall, and minor degrees of prolapse of the vagina when correctly performed, very completely restore anatomically the displaced and injured parts to normal position and function, and relieve the symptoms which have been dependent upon them. That this is true is evidenced by the fact of their almost universal adoption and practice by the American profession.

The surgical treatment of the lesser degrees of displacement of the uterus, retroversion and retroversion-flexion, and slight or early cases of downward displacement too, though still a question under discussion, is now very satisfactory.

There, however, still remains not a little dissatisfaction as to the treatment of the most distressing, serious, and intractable of the displacements of the uterus and vagina, namely, incomplete and complete prolapse or procidentia.

On the one hand the plastic operations which have been described and are generally performed for the cure of these conditions have not been adequately satisfactory; the retro-

[1] Read before the Southern Branch of the Philadelphia County Medical Society, March, 1906.

verted uterus again gradually descends down through the pelvis, and there is a return of the prolapse. As is shown, for instance, in the statistical study of Koblanck (*Zentralblatt f. Gynäkologie*, 1903, No. 27) that of 511 cases operated upon, but 44 per cent. remained free from a recurrence after a period of four years. In a large series operated upon in Hofmeier's clinic there was a return in 46.8 per cent. (Brandt, *Ibid.*, 1903, No. 36).

On the other hand the more radical form of treatment, the performance of hysterectomy, complete or with the elevation of the cervical stump, which has found so many enthusiastic advocates, does not ensure against recurrence of the vaginal prolapse. The statistics of Zolotarlyky (*Jahresberichte uber Geburtshilfe und Gynäkologie*, 1897, p. 96) show displacement of the vagina in 11 per cent., and a tendency to return in 15 per cent. of the cases operated upon, in all 26 per cent. in which the operation failed in its complete purpose. Further, hysterectomy, particularly the operation devised by A. Martin, C. Martin, and Edebohls, a panhysterectomy with excision of the vagina, is an operation associated with considerable danger to life, the mortality reported by the same authors, in a large experience, being 7 per cent. Doederlein (*Verhandl. der Gesellschaft f. Geburtshilfe u. Gynäkologie*, Würzburg, 1903) reports three deaths following operation among 63 cases, a mortality of about 5 per cent. In performing hysterectomy here incision is made through the œdematous and diseased prolapsed tissues, tissues the seat of a form of degenerative change, infection easily takes place (usually an infection virulent in character), and since the women are usually advanced in age with poor resisting power, the mortality after such a major operation must often be greater than statistics seem to point out.

What is of equal importance hysterectomy, even when successfully accomplished, is a mutilating operation which deprives the woman in the period of sexual activity of the power of procreation and of her other genital physiological functions (the Martin operation of sexual congress).

Hysterectomy is a radical and dangerous operation, never warrantable or necessary for the cure of uterine prolapse, and should be severely condemned.

A third method of surgical treatment is the combination of the operation of ventrosuspension or ventrofixation of the uterus with certain plastic operations on the cervix uteri and vaginal walls. While this operation is efficient, the extent of procedure, we believe, is rarely necessary or warrantable.

It is scarcely necessary to mention that mechanical supports and appliances, while indispensable in women who, either on account of advanced age, with great enfeeblement or because of serious visceral complications, cannot submit to operation without considerable risk to life, are mere makeshifts, at most extremely unsatisfactory, and, as will be shown, are not infrequently responsible for annoying and even serious injuries.

The method of treatment, whether medicinal, by mechanical appliance, or surgical operation, to be selected for the relief of any disease or condition which is a menace to normal health and endangers life, is that which combines the greatest freedom from mortality, the largest percentage of permanent cures, and the least inconvenience to the patient, and at the same time does not incapacitate or, if surgical, mutilate or deprive of normal physiological functions. Therefore, in the treatment of prolapse of the uterus if it be proven that these factors of true success are to be gained by extra-abdominal or plastic surgery performed on the uterus, vagina, and pelvic floor it is self-evident that they alone should be practised.

It is from this standpoint, and through these methods only, that I have thought the subject of this paper worthy of presentation and consideration before you.

In the discussion of the subject, I shall confine my remarks to the pathological anatomy and treatment of the common advanced forms of prolapse of the uterus and vagina, to those cases of displacement in which the uterine cervix protrudes beyond the ostium vagina, with or without supravaginal elongation of the cervix, the conditions known as incomplete and complete prolapse or procidentia.

During the last eleven years we have made a careful study of a comparatively large number of these cases at the Gynecean Hospital and Hospital of the University of Pennsylvania and practised a form of preparatory and operative treatment which has resulted, as time has proven, in attaining the most satisfactory results.

To appreciate the influence and to properly practice operative methods aiming to permanently cure a prolapsed uterus, we believe it is of the greatest importance that the surgeon be familiar with the etiology and process of descent of the uterus, the secondary pathological changes taking place in the prolapsed structures, and the involutionary changes to be gained by operation. Also, the complete success of the operations which shall succeed in permanently retaining the uterus in position is to a great extent gained through the personal judgment of the surgeon and what may be designated as the smaller details of his operative technique.

Without going into detail it may be stated that the primary etiology of descent of the uterus to the position of prolapse is dependent upon three forms of relaxation of the uterine and vaginal supports: first, relaxation of the supports of the pelvic floor or diaphragm, resulting from injuries, loss of rigidity, muscular weakness or atrophy of its contained or surrounding structures; second, relaxation of the uterine ligaments from any cause; third, relaxation, loss of rigidity or muscular weakness of the abdominal parietes.

One, two, or all three forms of relaxation may be present and operative in the individual case, the action of the one usually predominating that of the other. With the presence of one or more of these causes the normal pelvic equilibrium is destroyed, the uterus falls to the position of retroversion, and the intra-abdominal pressure acting from above with no resistance from below the uterus is slowly driven along the vaginal canal.

Subinvolution is often an added factor in the production of the retroversion. Such primary descent is secondarily influenced by the time increase of one or more of the forms of relaxation; by stretching of the uterine ligaments, the secondary pathological changes resulting from the descent which increases the weight of the uterus, and the dilatation of the vaginal canal. With the atrophic changes of advanced age there is less resistance to the descent of the uterus and it advances more rapidly. This accounts for the greater frequency of prolapse of the uterus after the menopause (fifty-nine of seventy-two cases). In this way the descent of the uterus and vagina slowly advance until complete or treated.

The character and extent of change, pathological change, in the uterus and vagina, the form of prolapse, depends upon the prominence, absence or presence of the relaxation, on the one hand, of the supports of the pelvic floor, or on the other hand of the intra-abdominal or abdominal wall support. Thus, where the greatest relaxation is in the pelvic floor there results a primary prolapse of the vagina, which then dragging on the cervix uteri while the uterine ligaments still remain suspensory, produce an elongation, stretching out, of the supravaginal cervix and finally a secondary prolapse of the uterine body. In the by far greater number of cases the vaginal character of prolapse predominates.

Where the greatest relaxation is resident in the uterine ligaments the uterus is displaced to the position of retroversion and then to prolapse by the action of the intra-abdominal pressure, and little change takes place in the body of the uterus or supravaginal cervix. This form is very rare.

With the descent of the uterus the vagina is inverted, the bladder, being strongly attached to the cervix and vesico-vaginal connective tissue, usually follows in the descent, is prolapsed with the vagina, protruding through the vaginal orifice. The rectum also, but less frequently, is prolapsed in the same manner.

Pathological or secondary changes, as a rule, take place in the prolapsed structures, resulting from inactive circulation in the pelvic bloodvessels and to a great extent through compression of the pelvic veins. There is a venous stasis or passive hyperæmia, followed by hypertrophy and to some extent hyperplasia of the prolapsed structures. If the uterus is removed in the common case of complete prolapse it is found to have a characteristic shape (Fig. 1). The infravaginal cervix instead of being the smallest portion of the organ is much the largest, often being three or four times its normal size and almost twice the size of the uterine body. The supravaginal cervix is greatly elongated and increased in diameter. Also, the body of the uterus is enlarged and thickened. The entire uterus may measure seven or eight inches in length, and is correspondingly broad. The endometrium is succulent and infiltrated with serous fluid, sometimes hypertrophied and not infrequently has the appearance and presents the microscopic changes of hyperplastic endometritis.

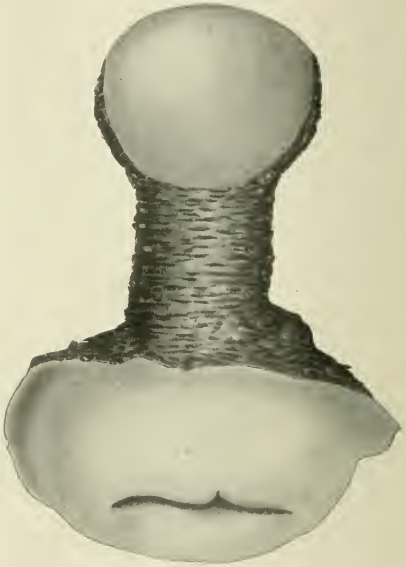

Fig. 1

A microscopic study of the tissues of the uterus shows simple œdema and hypertrophy, rarely inflammatory changes. The vaginal walls are greatly dilated, thickened and œdematous, with the epithelium dry and horny. Ulcerations of the vagina and vaginal cervix are often found, resulting from insult and poor nutrition.

As said, the appreciation of these anatomical and pathological changes, and their action in the production of the

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descent is of the greatest importance in considering and applying the treatment of this condition.

Knowing that the displacement results from relaxation of the uterine and vaginal supports, disturbances of the normal equilibrium of the uterus and secondary changes in the uterus and vagina, the cure will naturally depend upon: first, the relief of the secondary pathological changes; second, the completeness of reconstruction of normal or the formation of artificial supports to the uterus and vagina; and third, through this means the restoration of the normal equilibrium of the pelvic cavity. In other words, the treatment should be directed toward the relief of the pathological conditions in the order opposite to which they occurred.

Referring to the pathological anatomy, we find that the venous stasis, œdema, and hypertrophy present in all prolapsed structures is only induced by the presence of the prolapse, acting by compression of the veins of the pelvis and uterus. Therefore, it must be at once recognized as a fact that if the uterus and vaginal walls are even only temporarily replaced the normal relation will soon be restored, and with it the œdema and hypertrophy of all structures will rapidly disappear. The organ and tissues will return to normal size and proportion. Also, the dilatation action of the uterus being removed the vagina will contract. The attaining of such involuntary changes before attempting to restore the supports offer the valuable advantage that the surgeon at the time of operation is better able to determine the proper extent of operation on the cervix uteri which will secure atrophy of the entire organ, the extent of denudation on the anterior and posterior vaginal walls, and the amount of underlying tissue to be included to reconstruct strong, efficient vaginal supports.

With this end in view it is always our custom to plac the patient suffering with prolapse of the uterus on a preparatory treatment, until very complete retraction and contraction of all structures take place. This treatment consists in first replacing the uterus in the knee-chest position and keeping it in place by having the patient remain in bed, in the recumbent position or in the Sims position, for a period of from five to ten days. If the prolapse at any time recurs, as for instance through straining at stool, it is immediately reduced by the patient or a nurse. So as to be sure the uterus is always well within the pelvis it is advisable to instruct the patient to assume the knee-chest position two or three times each day for from five to fifteen minutes; second, a vaginal douche of a gallon or more of hot bichloride solution (1:4000) is administered twice daily. The intestinal contents are kept soft by laxatives.

The result of this preparatory treatment is at once most striking. A uterine cavity which measures five to six inches in length will be reduced to three inches, and if the treatment is kept up sufficiently long to two and a half inches (normal). There is also the same degree of contraction of the uterine and vaginal walls. Ulcerations of the cervix and vaginal walls, though extensive before the instigation of the treatment, rapidly heal. In passing I may add that such a preparation should be practised before introducing a pessary to retain a prolapsed uterus in position. It will prevent ulcerations and other complications.

Having gained every advantage of this preparation, the next step in the treatment must be to secure permanent involution of the uterus and vagina, and reconstruct the supports of the pelvic floor and vaginal outlet. It would seem advisable to also restore the intra-abdominal support of the uterus, securing the uterus in the position of anteflexion through an abdominal operation, but in our experience this has been very rarely necessary. The anteflexed position of the uterus is efficiently gained through the plastic operations to be described.

Permanent involution and even very marked atrophy of the uterus is secured by the operation of amputation of the cervix uteri and the restoration of the uterus to normal position. The method of amputation of the cervix uteri which has proven most satisfactory, is that devised by A. Martin, a description of which is to be found in many text-books. In performing this operation the largest possible amount of vaginal cervix is removed, the vaginal walls being dissected from the cervix up toward the internal os. Cumol-formalin catgut suture material, secured with shot, is employed. Where the uterus and cervix are atrophied, and there is no supravaginal elongation of the cervix, then amputation is not necessary, yet in many of these cases it is a safer plan to remove the cervix. It being remembered that we amputate the cervix to secure permanent involution of the uterus, diminish its weight and thus lessen the tendency to prolapse.

After this part of the operation has been carried out the uterus is dragged down through the ostium vaginæ by an assistant making traction on the cervix sutures. The operator then catches a point on each side of the cervix, about one-fourth inch above the position of the line of shotted sutures in the amputated cervix, and as far to the right and left of the cervix, over the position of the anterior surface of the base of the broad ligaments in the latero-anterior vaginal wall, as in his judgment can be brought together in the median line without undue tension when the uterus is replaced. This point on each side is about three-fourths of an inch distant from the lateral wall of the cervix, the three-fourth inch of tissue being over the position of the connective tissue of the base of the broad ligaments.

These points are then secured by double tenaculæ and form the starting point and extreme lateral limit of the denudation of the anterior vaginal wall. A strip of tissue is then denuded

from each starting point, gradually approaching each other until they meet at a point about one-fourth inch from the external urinary meatus. The lateral line of denudation is made well out to the left and right on the anterior vaginal wall, and turns rather abruptly toward the centre line as the urinary meatus is approached. Over the position of the muscle of the urogenital trigonum (Waldeyer) the denudation is made abruptly outward on each side, forming here a half-circle a half-inch in diameter, so that this muscle can be caught and brought together in the median line. The intervening mucous membrane is removed in strips, making the denuded area over the entire anterior vaginal wall triangular in shape, the base being just above and on a line with the shotted cervix sutures, and the apex one-fourth inch posterior to the external urinary meatus. In making the denudation the tissue is removed to the extent of exposing the bladder wall.

I would call attention to the fact that in relation with about that fifth of the denudation forming the base of the triangle, the denudation extends laterally three-fourths of an inch beyond the limits of the cervix and uncovers for suture this extent of the tissue of the base of each broad ligament.

This triangular area of denudation is closed by silkworm-gut sutures passed transversely. The first two or three sutures, beginning at the base of the triangle, are of the greatest importance. The silkworm-gut suture, armed with an Emmet round-pointed perineum needle, is made to pierce the vaginal mucous membrane a fourth-inch beyond the limits of the edge of denudation on the right, is carried rather deeply to grasp considerable of the connective tissue of the broad ligament, proceeding it is made to pierce, but not so deeply, the muscle tissue of the cervix (following the line of the base of the triangle), then in a like manner grasps the tissue of the broad ligament and the mucous membrane on the left.

The next one or two sutures are introduced in an identical manner, except that perhaps the third suture at its level includes the muscular wall of the bladder instead of that of the cervix. The sutures above these, toward the apex of the triangle, are introduced about one-fourth of an inch apart and include the mucous membrane and muscular wall of the bladder. Those introduced over the position of the muscle of the urogenital trigonum are made to include this muscle. After all of the sutures have been introduced the uterus is replaced and the sutures secured by shot (Fig. 2).

The points to be emphasized in the practice of this operation are: the primary selection of the points of lateral limit of denudation at the base of the triangle; the extension of the denudation well to the right and left over the position of the base or uterine attachment of the broad ligaments; the deep introduction of the first three sutures into the connective tissue forming the anterior portion of the base of the broad ligament, so as to grasp, suture over the cervix and shorten the broad ligaments; the introduction of the first two sutures into the muscle tissue of the cervix; all other sutures through the muscular wall of the bladder and the accurate apposition of the mucous membrane over the denuded surface without undue tension with the uterus in normal position. The objects of the operation are: the crowding of the cervix uteri backward and upward into the posterior vaginal vault; the whole uterus upward into the pelvic cavity, and the body of the uterus forward in normal anteflexion; the shortening of the strongest natural supports of the uterus, the broad ligaments; the narrowing of the anterior vaginal wall and the formation of a strong fold of support in the anterior vaginal wall through the inclusion of the muscular wall of the bladder. Immediately after the sutures are secured the uterus is found forward in a position of strong anteflexion, the operation acting as a form of vaginal forward fixation of the uterus. Further, it is now impossible to drag the uterus downward even a distance of half an inch, and with the suture of the bladder wall, including anteriorly the muscle of the urogenital trigonum, any sagging downward of the anterior vaginal wall is prevented.

Assuming that the theory of Veit and Schroeder is correct, that the progress of prolapse of the uterus is dependent to a great extent upon and occurs only concomitant with prolapse of the anterior vaginal wall, this operation, agreeing with Fehling, offers the correct principle and is a most efficient support. This operation, practised as described for the last five years, has a similar principle to that recently described by Reynolds, and is practised by Dudley, of Chicago, except that it is more extensive and effectual, and that it also aims to carry the body of the uterus forward in normal position.

Finally, it is necessary to restore the supports of the pelvic floor, the levator ani muscle and pelvic fascia, forming a more than normally strong and complete pelvic diaphragm. Also to restore the vaginal outlet to normal size. The completeness of this part of the operation is likewise of the greatest importance in supporting the anterior vaginal wall and maintaining the uterus in position.

Since the pelvic diaphragm has usually been lacerated years before, the tissues have retracted, then through loss of function and often also through the climacteric changes and other influences, have atrophied, the relaxation is extreme. The Emmet operation for repair of the perineum would therefore prove insufficient. The method of procedure which we have here found to meet every indication is a modification of the Hegar perineum. A triangular denudation is made on the posterior vaginal wall in the usual position for the repair of the perineum. The apex of this triangular denudation extends upward toward the cervix for

a distance of about three inches. The base is at the fourchette. The lateral denudation is extended to a point on each side, which, when the denuded surfaces are brought together, will narrow the vaginal canal and orifice to the size of the index finger. The surgeon determines the extent of this lateral denudation by, from time to time, bringing the edges together by means of forceps. The apex of the triangle for a short distance is then closed with cumol-formalin catgut.

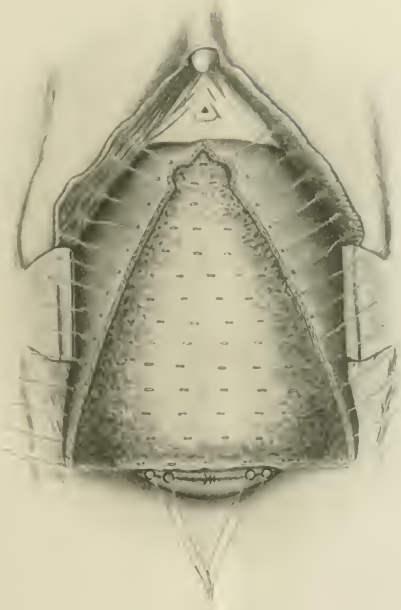

Fig. 2

Then silkworm-gut sutures are introduced transversely and from above, downward and inward, traverses the centre of denudation, and then outward and upward, to emerge on the left opposite to the point of entrance. In the placing of these sutures the Emmet perineum needle is introduced deeply from above downward and outward on the right, catching a large portion of the fibres of the levator ani muscle and pelvic fascia, more superficially over the position of the rectum, then from below outward and upward on the left to catch the same amount of muscle tissue and fascia on the left. Each suture, proceeding from apex to base of the triangle, is introduced and immediately shotted, so that the succeeding suture catches the tissue at a lower level than would otherwise be possible. The vaginal orifice, as said, is in this way narrowed until it only admits the index finger. An artificially strong, high and broad pelvic diaphragm is formed, composed of each lateral half of the levator ani muscle and the surrounding pelvic fascia, united in the median line. A gauze drain is finally introduced into the vagina (Fig. 3).

The after-treatment consists simply in the administration of a large hot daily sterile water vaginal douche, and the keeping of the patient in bed in the recumbent position for four weeks. The perineal sutures and those in the anterior vaginal wall are removed at the end of three weeks. The catgut sutures in the cervix are absorbed after a few days, and the shot come away.

Two or three weeks after the sutures have been removed

sufficient relaxation is found to have taken place to make the vagina a little less than normal size. We have now performed these operations in seventy-two cases, with, as far as we can learn, the most satisfactory results.

The uterus was completely prolapsed and the vagina completely inverted and prolapsed in forty-five cases, and incompletely prolapsed, the cervix extending one or more inches beyond the ostium vagina in twenty-seven cases. In all but one the convalescence was uncomplicated and easy, the patients always being quite comfortable after twenty-four hours. In the one case pneumonia was a complication, the patient recovering.

Fig. 3

Eleven years have elapsed without recurrence in two cases, nine years in seven, eight years in ten, seven years in eight, six years in six, five years in six, four years in six, three years in six, two years in three, one year in eight, and less than a year in nine.

A recurrence took place in one case after a period of two months. In this instance the prolapse was extreme, had existed for a great many years, and there was a complete atrophy of all muscular and fascial supports. It was our judgment at the time of operation that no muscular or fascial supports were being or could be grasped in the sutures to sufficiently support the uterus and vagina. Further, it was one of our early cases, operated upon before the procedure which includes the base of the broad ligaments in the suturing, as described, was devised. Recurrence, therefore, took place in one of seventy-two cases, or in one and one-fourth per cent.

The ages of the patients at the time of operation varied between twenty-eight and seventy-one years, as follows: between twenty-eight and thirty-five, four; thirty-five and forty, twelve; forty and forty-five, six; forty-five and fifty, six; fifty and fifty-five, fifteen; fifty-five and sixty, twelve; sixty and sixty-five, sixteen; sixty-five and seventy-one, six.

It was necessary to amputate the cervix in fifty-nine of the cases.

Ventrosuspension was an accessory operation in four cases, being employed in two women, where the described narrowing of the vagina could not be carried out, and in the other two because it was necessary to open the abdomen to perform bilateral salpingo-oöphorectomy for pyosalpinx.

Diabetes was a complicating disease in two, and chronic opium poisoning in two cases. In one case, a woman thirty-five years of age, where the uterus had been completely prolapsed, causing sterility for five years, impregnation occurred one year after operation, she went to term and I delivered her of a living child. The labor was uncomplicated and the perineum only slightly torn. Five years have passed since the birth of her child and the uterus still remains in good position.

The advantages of these forms of operative methods from this study are as follows:

1. That it is an operation wholly free from danger, all patients having an easy surgical convalescence. Pneumonia developed in one case.

2. That it has been a complete success in every case thus far operated upon, no recurrence having taken place since the adoption of this particular operation.

3. That it is not a mutilating operation, as it leaves every organ intact.

4. That it does not in any way disturb physiologic functions and destroy the sexual relations between man and wife.

5. That when performed before the time of the menopause it affords the possibility of impregnation, normal pregnancy and labor without a recurrence of the prolapse.

6. That it can be performed with safety at any age.

The contraindications are great enfeeblement of old age, the prolapse of the uterus being of secondary importance, chronic heart, kidney, liver and lung disease, inflammatory disease of the Fallopian tubes unless treated at the same time, suppurative parametritis and abscess formation, perimetritis, advanced cystitis, ureteritis, and pyelitis, and carcinoma of

the uterus and vagina. That prolapse of the uterus is a condition always demanding surgical treatment, there can be no doubt; particularly if the results here reported are to be obtained.

As stated in the beginning, the use of mechanical appliances and supports are mere makeshifts, are very annoying, and often responsible for serious injury. Through pressure necrosis and ulceration such appliances have frequently produced rectovaginal and vesicovaginal fistulæ.

Neugebauer has collected 242 cases from the literature in which a pessary ulcerated or necrosed into the neighboring important tissues or organs, as the parametrial tissue, bladder, rectum, and uterus, such injuries in many instances resulting in death. Zwanke states that serious injuries follow the use of the pessary in 10 per cent. of the cases in which it is employed. In the case where a pessary must be employed, because of feeble old age or because of serious visceral complicating disease, the Thomas or Smith instrument should be selected, and one of these failing to keep the uterus in position Braune's colpeurynter is most satisfactory. Such instruments should be removed, cleansed, and reintroduced at frequent intervals.

Aside from the injuries due to the use of the pessary, serious and often fatal complications frequently result from the presence of the prolapsed uterus, vagina, and bladder. Frequently there is a catarrhal cystitis, sometimes followed by inflammation and necrosis of the bladder mucous membrane and muscle wall; or extending from the bladder there is a ureteritis, pyelitis, and surgical kidney. According to the statistics of Kustner forty to eighty per cent. of the cases have inflammation of the ovaries, tubes, or pelvic peritoneum, and thirty-three per cent. periuterine adhesions. Severe septic infection, abscess formation in the pelvic connective tissue, especially that between the bladder and the uterus, has not rarely been described; also, abscess formation in the uterine muscle, tubes, and ovaries. Such infection and abscess formation is usually followed by localized or general peritonitis and death. We have observed two cases die of septic infection of the urinary tract, two from general peritonitis resulting from rupture of a pyosalpinx in the replacing of a prolapsed uterus, and another from incarceration, streptococcus infection, and abscess formation in the uterus, perivesical tissue, and general peritonitis.

The danger in every instance of prolapse of the uterus and its palliative treatment is sufficient to warrant the early performance of the plastic operations here described.

NOTES UPON THE CLINICAL EXAMINATION OF THE FECES.[1]

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I. A CASE OF POOR DIGESTION OF MUSCLE FIBRE DUE TO REFLEX INTESTINAL IRRITATION FROM CHRONIC APPENDICITIS.

(From the Service of Professor Musser, Hospital of the University of Pennsylvania).

The recent advances made in our knowledge of the physiology of the gastrointestinal tract have made it increasingly difficult to utilize the feces as an index of the activity of the pancreas and intestinal glands. The digestive processes to which any substance is subjected during its passage through the gastrointestinal tract are very complex, and the secretions of the different organs are markedly interactive. Thus the presence of fat in the stool, which was formerly thought to be an important sign of pancreatic disease, loses all its significance if the flow of bile is interrupted, as it so often is in diseases of the pancreas. Deficient splitting may be due to the entire absence of pancreatic secretion or to the lack of the intensifying action of the bile, and therefore neutral fat in the stool loses its value as a sign of pancreatic disease when no bile is entering the intestine.

In somewhat the same manner the activity of the pancreatic secretion depends upon the intestinal secretion. When the pancreatic juice enters the intestine it contains no active proteolytic ferment. The conversion of trypsinogen into active trypsin is dependent upon the activating ferment entrokinase, which is found in the secretion of the intestinal glands; consequently when the activity of the intestinal glands is interfered with the proteolytic action of the pancreas must be as effectively prevented as if the pancreatic secretion itself was suppressed. Therefore, a pathological amount of muscle fibre in the stool might mean either absence of trypsinogen or of its activating ferment, entrokinase.

The following case is a very good illustration of the difficulties of interpreting the findings in the stool in examinations of cases of gastrointestinal disease. Here the presence of pathological amounts of muscle fibre probably meant the suppression of the secretion of the intestinal glands and not

[1] Read before the Association of American Physicians, Washington, May 16, 1906.

the absence of trypsinogen. It is also an interesting example of intestinal disturbance, produced apparently reflexly by a chronic appendicitis.

Case 10. Male, aged twenty-three years, white, farmer.

Diagnosis. Diarrhœa due to azotorrhœa; chronic appendicitis. Operation, with removal of appendix. Subsequent ability to eat meat without diarrhœa.

Summary. He had had an attack of diarrhœa and abdominal cramp nine months before. Since then there have been very frequent attacks of diarrhœa and progressive loss of weight. After admission to the hospital it was discovered that his diarrhœa was apparently caused by poor digestion of muscle fibre. When he took two hundred grains of broiled beefsteak pieces of muscle fibre visible to the naked eye were very numerous in his stool. Starch and fat digestion and absorption were good. No nuclei were found in the meat. Gastric digestion and secretion good. When meat was dropped from the diet the diarrhœa stopped and the patient gained thirty pounds upon a diet consisting of vegetables and fat. His improvement lasted for three months, but the diarrhœa returned whenever he ate red meat. After three months he had an attack of appendicitis and was operated upon. The appendix was found to be the seat of the chronic inflammation and was tightly bound down by adhesions. It was removed. Since the operation he can eat meat without diarrhœa, and an examination of his stool after the ingestion of 200 grams of rare broiled steak showed no visible pieces of meat fibre. The connection between the azotorrhœa and chronic appendicitis seems too definite to be merely a coincidence.

O. T., male, aged twenty-three years, white, farmer. He never used tobacco or alcohol, and denies venereal disease. He always has had a good home and regular, good meals. In October, 1904, after indulging in sweet cider, he was seized with diarrhœa and abdominal cramps, which at first were most severe in the epigastrium and then spread to the lower and central abdomen. These cramps came on irregularly and without relation to the taking of food. They were accompanied by gaseous eructations and distention. The diarrhœa was constant with an average of four or five watery stools daily. Occasionally there was a little blood and mucus mixed with the feces. He lost steadily in weight and fell from 145 to 118 pounds. He was never jaundiced. There were no symptoms referable to the urinary, vascular, or nervous systems. He was admitted to the medical wards of the University Hospital, in the service of Dr. Musser, June 10, 1905.

Examination upon admission showed a somewhat tense and moderately contracted abdomen. There was no tenderness except in a spot in the middle of the epigastrium and the recti muscles were rather more tense over the upper half of the abdomen. The teeth and mouth were normal. The organs of the thorax were normal.

Stomach. An Ewald breakfast showed good digestion: t. a., 44; free hydrochloric acid, 20. No retention. Inflation of the stomach showed that it was normal in size and position.

Blood. There was a moderate secondary anæmia. Hæmoglobin 85. No leukocytosis. Urine normal in amount and constituents.

Tuberculin test negative, excluding tuberculous enteritis.

Fever. The patient had no fever while under observation.

Proctoscopic examination was negative.

Feces. Examination while the patient was upon beef-broth and milk diet showed absence of mucus and no occult blood. There were numerous undigested muscle fibres in the stool, although the patient had had nothing made from meat except broth for a week. The fibres did not contain nuclei. Occasionally while under observation there was a little mucus in the stool.

June 15. The patient was placed upon the writer's modification of Schmidt's test diet. This showed a period of passage of thirty hours. Muscle fibres were present in great excess, and were visible to the naked eye. Connective tissue was found only microscopically and in small amounts. No potato cells nor starch. A very moderate amount of fats. No starch fermentation or albumin putrefaction. Reaction neutral or slightly acid. Sublimate test showed hydrobilirubin. No mucus. No blood. No parasites. The patient was kept upon this dict for five days and the fact was clearly established that digestion of meat fibre was very deficient, while that of starches and fat was very good. No muscle nuclei were found at any time.

The patient was put upon a diet containing no meats and with an increased amount of starch and butter fat. Under this dietary the diarrhœa stopped and the body weight began to increase, confirming the supposition that the diarrhœa was connected with the undigested meat.

Examination of the stool showed that the extra starch and fat were well borne, but whenever he was given a piece of meat, muscle fibre visible to the naked eye appeared in the stool. The patient was then put on a diet containing a still greater amount of starch and fats and was given a half-ounce of pure olive oil after each meal, which was later increased to one ounce. When he left the hospital he was taking 2 quarts of milk, 6 eggs, 300 grams of rice or potatoes, 6 pieces of toast and butter, besides the regular vegetables and desserts of a house diet, with 3 ounces of olive oil daily. His stools showed: considerable soap but no neutral fats; no excess of starch; no starch fermentation; no albuminous putrefaction. The sublimate test showed hydrobilirubin. Reaction acid. The patient's weight had risen from 112½ upon June 19 to 118½ upon June 25. He

B. J. C.

was instructed to adhere to this diet and was discharged. A note from him a month later said that he had gained 28 pounds (weight 141), and was free from diarrhœa and symptoms of enteritis.

After leaving the hospital he kept fairly comfortable as long as he did not eat meat. His diarrhœa returned whenever he ate broiled beefsteak or chicken or even beef- or chicken-broth.

On September 1 the patient developed symptoms of appendicitis and was operated upon by Dr. Cullen, of Baltimore, who reports to me that the appendix was nearly twice the usual length, and was glued down by adhesions throughout almost the whole course. There was some thickening of the colon but no adhesions elsewhere. The case was undoubtedly one of appendicitis that had lasted over some time, as the inflammatory process was chronic. Since the operation the patient improved very rapidly, and between September 2 and December 1 had risen to 139 pounds. He reported to me that now he could eat meat with impunity.

In order to determine whether the operation had had any real effect upon his azotorrhœa, I had him eat a quarter of a pound of rare steak and six ounces of mashed potato, and send me his stool next day. The examination showed abundance of muscle fibres microscopically but no visible particles. In other words his power to digest muscle had returned approximately to normal. The stool showed good starch and fat digestion and absorption.

2. OCCULT BLEEDING IN TYPHOID FEVER.

(From the Clinical Laboratory of the Presbyterian Hospital, Philadelphia.)

In a paper which appeared in 1905 (*American Journal of the Medical Sciences*, July, 1905) I reported a series of observations upon occult intestinal hemorrhage in typhoid fever.

I found occult bleeding only three times in ninety tests in nineteen cases, which was a surprisingly small proportion of positive tests, when it is considered that typhoid is a disease accompanied by ulceration of the bowels.

During the past winter I have studied thirty additional cases more or less systematically. As in my first series, the tests were always made in the febrile period of the disease. The results of my second series of observations were strikingly different from my first and showed a much larger percentage of positive occult blood tests. I have combined the two series and now report the results of two hundred and thirty-nine observations upon forty-nine cases.

The tests were made with due regard to the presence of hemorrhoids, of swallowed blood and of the use of beef-juice as a food. To obtain reliable information the examination should be systematic and should be made upon every stool.

The method used was the guaiac-peroxide and aloin-turpentine tests made upon an acetic acid-ethereal extract of the stool. The technique is given in full in my paper, to which I have referred.

I found occult bleeding thirty-two times in two hundred and thirty-nine stools tested in the forty-nine cases. The number of patients showing positive tests was fifteen, or 29.5 per cent. of the total forty-nine cases. Occult bleeding occurring within three days after a visible hemorrhage was not tabulated, for the blood from the visible hemorrhage would probably not leave the gastrointestinal tract in less than three days.

The percentage of positive cases in the combined series is much larger than in my first series and probably gives a more correct idea of the frequency of occult bleeding in typhoid. My percentage is slightly lower than that given by Petrachi or Romani, who have also published series of observations on the subject.

Petrachi (*Zeitschrift f. klinische Medizin*, 1905, vol. lvi.) found occult bleeding in forty-four per cent. of eighteen cases.

During the past year Romani (*Riforma Medica*, February 3, 1906) has published the results of a series of observations in which he found occult bleeding in thirty-two per cent. of fifty cases.

My percentage of positive cases agrees quite closely with that of Romani in about the same number of cases. Both of our series are larger than that of Petrachi, and therefore are presumably more accurate and indicate, in round numbers, that occult bleeding occurs in a third of all cases of typhoid.

Most of my tests were made in the second, third, and fourth week of the disease, and the greatest number of positive results were obtained, as would be expected, in the third week.

The proportion of positive tests in relapses was greater than in the primary attack although the number of observations is too small to be conclusive.

The following table shows the number of tests and the positive results by weeks of the disease:

First week	1 stool tested.	negative.	
Second week	51 stools tested.	6 positive.	
Third week	64 " "	9 "	
Fourth week	70 " "	5 "	
Fifth week	26 " "	5 "	
Sixth week	14 " "	3 "	
Seventh week	8 " "	4 "	

Relapses:

First week	3 stools tested.	2 positive.	
Second week	1 stool tested.	1 "	
Third week	1 " "	1 "	
Fourth week	1 " "	1 "	

In my series occult bleeding occurred quite as often in mild as in severe cases and, as has been said, is very likely to take place during a relapse.

My observations, therefore, do not agree with those of Petrachi, who says that the occurrence of bleeding varied directly with the severity of the attack.

Romani, however, found, as I did, that occult bleeding occurs quite as often in mild cases as in the severe ones.

The following table shows the severity and the proportion of occult hemorrhages:

Mild	13 cases,	5 positive
Moderate	20 "	2 "
Severe	13 "	6 "
Relapses	2 "	2 "

In judging the severity of the attack the amount of toxæmia and the duration of the fever were taken into consideration. Probably no correct idea of the frequency or causes of occult bleeding in typhoid fever will be obtained until many series of observations are compared from hospitals who have all sorts of cases and where different varieties of treatment are in force.

The cases at the Presbyterian Hospital, where my work was done, as a rule come from a comparatively prosperous class of mechanics, who enter the hospital fairly early in the course of the disease. The treatment consists of a minimum of drugs, baths, or sponges for the fever and a liquid or very soft diet.

The typhoid mortality for the last ten years, including moribund cases, is 12.2 per cent. It would be interesting to know what the frequency of occult bleeding is in hospitals where the patients come from the poorest classes and when the disease is neglected and allowed to run a good part of its course before admission.

The practical usefulness of the detection of occult bleeding in typhoid would seem to lie in the possibility of foretelling visible hemorrhage by occult bleeding.

In my experience occult bleeding does not precede visible hemorrhage with sufficient regularity to make the test of much practical value. On the other hand, visible hemorrhage does not always follow occult bleeding. In a general way, however, it may be said that those cases that show a tendency to occult bleeding are the ones in which visible hemorrhage is most likely to occur.

Among the fifteen cases with occult bleeding, six had visible hemorrhage. On the other hand, of the ten cases with visible hemorrhage four cases did not show occult blood except directly after the visible bleeding.

The following cases are the best examples of the close association of occult and visible hemorrhage:

Case B.—Male, aged thirty-nine years.

Nineteenth day	Occult blood
Twentieth day	Hemorrhage
Twenty-fourth day	"
Thirty-fifth day	Negative
Thirty-sixth day	Occult blood
Thirty-eighth day	" "
Fortieth day	Hemorrhage
Forty-second day	Occult blood
Forty-fourth day	" "
Forty-sixth day	" "
Forty-seventh day	" "
Fifty-second day	" "

McM., female, aged thirty-eight years.

Sixteenth day	Occult blood
Seventeenth day	Hemorrhage
Twenty-first day	Occult blood
Thirtieth day	" "
Thirty-first day	Hemorrhage
Thirty-seventh day	Occult blood
Fortieth day	" "
Forty-third day	Negative
Forty-eighth day	"
Forty-ninth day	"
Fifty-second day	"

An example of a case in which hemorrhage may occur without warning is the following:

C. C., male, aged thirty-four years.

Twenty-first day	Stool negative
Twenty-second day	"
Twenty-third day	"
Twenty-fourth day	"
Twenty-fifth day	"
Twenty-sixth day	"
Twenty-seventh day	"
Twenty-eighth day	"
Twenty-ninth day	Hemorrhage
Thirtieth day	"
Thirty-fourth day	"
Thirty-sixth day	"
Thirty-seventh day	Occult blood
Thirty-eighth day	Negative
Thirty-ninth day	"

Both Petrachi and Romani claim that their observations showed that occult bleeding always preceded visible hemorrhage by from one to five days and by this means it is possible to prophesy serious hemorrhage. However, neither says how often in their experience occult bleeding was not followed by hemorrhage.

Upon the whole it may be said that occult bleeding is not as common in typhoid fever as might be expected. The typhoid ulcers seem to show less tendency to bleed than do other ulcers of the gastrointestinal tract, and this is an interesting side-light upon the pathology of the disease.

Thus far one cannot hope for much aid in diagnosis or conduct of the treatment by the systematic examination of the stools for occult blood.

FURTHER EXPERIMENTAL INVESTIGATIONS INTO THE GROWTH OF TUMORS. DEVELOPMENT OF SARCOMA AND CARCINOMA AFTER THE INOCULATION OF A CARCINOMATOUS TUMOR OF THE SUBMAXILLARY GLAND IN A JAPANESE MOUSE.

By Leo Loeb, M.D.,
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(From the Pathological Laboratory of the University of Pennsylvania).

The experiments in the following report were carried out during the spring and summer of 1904. A short time ago Ehrlich[1] published two important papers giving observations on experiments in many respects similar to the ones made by myself.[2] Nevertheless, there are some important features which distinguish my findings quite markedly from those of Ehrlich and which may not be without interest at this time.

In the beginning of March, 1904, I obtained a female Japanese mouse with a small tumor in the upper part of the neck. It was a little smaller than an almond plus its shell and somewhat larger than a lima bean. As far as I could learn the animal was six to eight months of age. At two months of age the tumor was first observed. About a month later the solid white tumor was excised. One month later it began to grow again and gradually increased to double its original size in about four months after its appearance, its growth being slow. When I obtained the animal it was in good physical condition, the tumor being movable with the skin and without ulceration. March 12, 1904, the tumor was cut out and from three parts of it pieces were taken for microscopic examination, the rest of it being cut into small particles and a suspension of them injected into a number of Japanese and white mice.

Eleven Japanese and six white mice were injected, mostly in the subcutaneous tissue of the back. Part of the suspension of the tumor was twice filtered through dense filter paper and injected into three Japanese and two white mice.

Before I report the results of the inoculation I will briefly indicate the character of the submaxillary tumor, a more detailed description being given later. The tumor had a gland-like arrangement; ramifying ducts were surrounded by alveolar structures; it was embedded in the tissue of the submaxillary gland. Two varieties of cell were present: cuboidal or cylindrical epithelial-like cells which formed alveoli filled with colloid material, and cells which had a finely or coarsely vacuolated character. The latter cells seemed to have the same character and origin as the former cells; cells of a similar appearance may be found in certain glandular structures, as for instance in certain salivary and the sebaceous glands. Both varieties of cells were found mixed in the same alveoli. Some of the gland-like alveoli consisted entirely of vacuolated cells. Instead of colloid material in the centre of the alveoli, cells with large vacuoles were occasionally found, their subsequent liquefaction leaving cavities instead of colloid material. At other places both varieties of cells assumed a diffuse growth, connective tissue forming certain partitions.

In regard to the results of the transplantation, it is here necessary to be very brief. A number of the inoculated mice died very early and the pieces of the tumor were examined in different stages of development. Through an accident it was only possible to save two Japanese mice, which lived for several months after the inoculation. Both of these developed several tumors. From one of these tumors a new lot of mice were inoculated. In all of the inoculated mice, with the exception of those which died soon after the operation, tumors developed. In not a single instance did an inoculated white mouse develop a tumor. These results are perfectly in accord with my former results of transplantation of sarcomata. In those experiments white rats were used. Tumors could only be transplanted into white rats and into hybrids between white and gray rats. In mice inoculated with filtered fluid tumors did not grow. This observation likewise agrees with my former results. One mouse which had received beside the filtered fluid a piece of the tumor preserved for some time in glycerin developed a tumor. In this case the formation of the tumor was evidently due to the tumor material preserved in glycerin. In this case the inoculated tumor grew after a markedly prolonged period of latency. By the latter term the writer understands the period between the inoculation and the time at which the growth becomes macroscopically visible. This result confirms our former conclusions. Our previous experiments have shown that we are able to decrease the virulence of tumors materially by heat and by chemical means in a

[1] P. Ehrlich u. H. Apolant. Beobachtungen über maligne Mausetumoren. Berl. klin. Wochenschrift, No. 28, 1905; No. 2, 1906.

[2] These investigations were of course carried on quite independently of those of Ehrlich. After having noted the gland-like character of the original tumor, the first transplanted tumor examined microscopically was unexpectedly found to be a typical spindle-cell sarcoma. A report on these findings was announced on the program of the meeting of the American Association of Pathologists and Bacteriologists, spring, 1905. The writer was unable to be present at the meeting and the following communication was read at the Baltimore meeting of the Association of American Pathologists and Bacteriologists, May, 1906. A full report with drawings will be published later.

similar way, as it has been possible in the case of bacteria. It is possible to grade the decrease of virulence in such a way that the tumor is not yet killed but grows much more slowly and frequently begins to retrogress spontaneously. We also pointed out that these means might be used for the production of an active immunity. Ehrlich and Haaland confirmed in their recent publications these facts entirely; Erhlich was furthermore able to produce an active immunity.

An extended histological examination of each of the inoculated tumors, in some cases based on serial sections, led to the following observations: first, although the original tumor was uniform in character, in the transplanted tumors we find in each of the growing tumors (and each animal of the second generation had several growing tumors), in addition to the same gland-like structures, a typical spindle-cell sarcoma. In the third generation there was a similar combination of gland-like structures with sarcomatous portions present. In several mice the glandular structures were very large, in others they were smaller. In only one of them (an animal of the third generation) no gland-like structure was found, the tumor being entirely sarcomatous as far as the examination extended, a possibility being of gland-like structure existing in unexamined portions. In one mouse of the second generation a very slowly growing sarcomatous nodule was removed and was followed by a rapidly growing sarcomatous tumor. We had therefore to deal with true sarcomata. At one side of this recurring sarcoma a few alveoli of the glandular structure were observed. The sarcomatous structure originally only grew in connection with the gland-like tumor. The relative amount of each component part later differed in the various tumors—in some the gland-like formations predominating, in others the sarcomatous. These two structures were either sharply separated or the sarcomatous included the gland-like parts.

The appearance of a sarcoma after the transplantation of a gland-like tumor is very surprising. It might be explained in three ways:

(*a*) In the original tumor there was a sarcomatous component already present.

(*b*) The growth of the gland-like tumor was in some way the cause of the previously quiescent or only regenerating connective tissue assuming a sarcomatous growth.

(*c*) A transformation of the gland-like structure into spindle-celled tissue occurred, the latter being able to produce connective tissue fibres.

The first possibility can almost with certainty be excluded for the following reasons. Three parts from the relatively small original tumor were examined microscopically. They did not show spindle-cell sarcoma. Furthermore, several transplanted pieces were examined soon after the inoculation; spindle-cell sarcoma was nowhere present. On the other side, all of the growing tumors of the two mice of the second generation presented both sarcomatous and gland-like structures and to produce this result, according to the first explanation, each transplanted portion must have contained sarcomatous and gland-like components; this is extremely improbable if we consider the results of the microscopic examination of three different parts of the original tumor, and of those transplanted pieces which were taken out during the period of latency.

Which of the other two theories is the correct one cannot at present be decided with certainty. There are some reasons to be adduced for each, but time does not permit of a fuller discussion here. We shall later briefly indicate which of the two views has the better foundation.

The following observation may become of importance for further experimentation.

We have to deal in these transplantations with two varieties of tumors which are morphologically quite different: a gland-like tumor forming alveoli and a typical spindle-cell sarcoma, both growing separately or intermingled.

We observed very marked variation taking place in the rapidity of growth and in the period of latency in the three generations. The original tumor grew very slowly. In the second generation the period of latency lasted approximately two months, the growth afterward being very slow. In the third generation the period of latency was very brief, one to two weeks being the average time, relatively large tumors being present after two to four weeks.[1]

The great point of interest is that this difference in the rate of growth affected equally both sarcomatous and gland-like portions. In the second generation sarcomatous parts grew very slowly; in the third generation they grew very rapidly. In the original tumor and in the second generation the gland-like structures grew very slowly. In the third generation they developed on the whole much more rapidly.

The fact is the more surprising if we consider that the rate of growth observed in the sarcomatous and gland-like tumors of this series of transplantations differs markedly from the growth of the sarcomata used in my former experiments and also from the rate of growth of tumors which have been transplanted by other investigators. Nevertheless, the sarcoma and gland-like structures have in this series of transplantation an almost identical rate of growth in the different generations. It might be explained in two ways:

First, the sarcomatous tumor owes its existence to a transformation of a gland-like tumor. The common origin of both cells would explain their similar reaction as expressed in the variations of growth. Although a great similarity exists at certain places between the cells of the gland-like tumor and the interstitial cells, the sarcomatous tumor

[1] The significance of this fact has been pointed out in another place, and does not need to be entered here. American Medicine, vol. x., No. 7, August 12, 1905.

proper and the gland-like tumor do not show any direct transitions into each other.

The second possibility is the following: The gland-like tumor transmits something to the connective tissue which causes the latter to assume a sarcomatous growth. It is not necessary, as Ehrlich concluded from his observations, that connective tissue has to be transplanted through a number of generations before it can assume a sarcomatous growth. A stimulus can be transmitted to the connective tissue already in the second generation. I found, moreover, in experiments carried on during the last few years, and which shall be reported in detail later, that ordinary epithelium or connective tissue after a series of transplantations does assume a markedly increased rate of growth.

We have therefore to conclude that it is most likely that some agency is transmitted from the gland-like structure to the connective tissue and that this factor causing the increased growth of the connective tissue is identical with the factor responsible for the growth of the gland-like tumor. The same agency is, according to this interpretation, responsible for the growth of both tumors. It is moreover, likely that the connective tissue surrounding the gland-like tumor, and not the connective tissue which lies *between* the glandular structures, is the starting point of the sarcoma. We see, namely, in early stages the sarcoma developing at the periphery of the glandular tumor and not between it. It is therefore improbable that the transplanted stroma of the gland-like tumor itself assumes a sarcomatous growth.

A very striking difference between the tumors of the first and second generations on the one side and of the third generation on the other side, is the great uniformity in the histological structure of both the sarcomatous and gland-like tumors in the third generation and their polymorphous character in the first and second generations.

In the second generation the gland-like tumors grow in two different ways, new alveoli being created through the formation of cell nests of at first apparently undifferentiated cells which gradually form central cavities or colloid through transformations of the centrally situated cells. Secondly, we find that well-developed alveolar structures increase in size by mitotic cell division. In the third generation we find only the latter mode of growth to be present. The transformations of the cylindrical or cuboidal cells into vacuolar cells does no longer take place. In the second generation the sarcomatous cells are frequently polymorphous, in the third generation no such variations are found.

There is, however, one feature in common between Ehrlich's series and the one reported here: in both cases the sarcomatous part gradually crowds out the gland-like structures, so that we may assume that if the tumor had been transplanted into further generations—which was prevented by the inability to secure suitable Japanese mice, with the means at our disposal—that the gland-like structure would have gradually disappeared in time, leaving only a sarcomatous growth.

The observations recorded here may throw light on a very interesting variety of mixed tumor, consisting of glandular and sarcomatous structures, which has been mainly found in the thyroid of man as well as of several species of animals.[1] The sarcomatous part of such a tumor in a rat was used in a former series of the writer's transplantations.

It is not unreasonable to assume that in those cases of the mixed tumors of the thyroid we have also primarily to deal with the proliferation of the glandular structures and that some agency is transmitted to the connective tissue which causes it to proliferate.

Some of the conclusions drawn from the facts which mainly during the last seven years have been established through experimental investigations into the conditions of growth of tumors are necessarily merely of a tentative character; further experiments will be necessary to determine which of the possible explanations is in each the correct one; but much of the evidence submitted in this paper could be best explained by the assumption that a micro-organism present in, and responsible for, the growth of the gland-like structures was transmitted to the connective tissue and caused it secondarily to proliferate. The other explanations can, however, not yet be excluded with certainty.

CONCLUSIONS.

1. In the course of the transplantations of a gland-like tumor of the submaxillary gland spindle-cell sarcoma began to grow besides the tumors resembling the original growth. In the original tumor no spindle-cell sarcoma could be found.

2. The spindle-cell sarcoma was found already in the second generation, long-continued transplantation of connective tissue being not essential for the production of a sarcoma.

3. Transplantation of normal epithelium or connective tissue through several generations does not cause a noticeable increase in the rate of growth of such tissues.

4. The two varieties of tumor growing side by side follow the same variations in growth which were characteristic of the rate of growth in the different generations and both obtained equally in the course of transplantation an increased virulence.

5. The increase in the rate of growth is due to a direct stimulating effect either upon the two varieties of cells which are found in the gland-like tumor and in the sarcoma, or upon a micro-organism which is possibly the cause of the two tumors.

[1] Such cases have been described among others by Kaufmann, G. H. Wells, Saltykow and myself.

6. If we assume that a micro-organism is the cause of these tumors the facts found in this series of experiments can best be explained by the hypothesis that the *same* micro-organism originally present in the gland-like structure secondarily invades the connective tissue and causes it to assume a sarcomatous growth. A transformation of carcinomatous cells can, however, not yet be excluded with certainty.

7. Certain formative stages in the development of sarcoma and gland-like tumors were limited to the first and second generations and were no longer present in the third generation. This is probably due to the great increase in the rate of growth observed in the third generation.

8. The rate of growth of the sarcoma gradually exceeded that of the gland-like structures, so that in all probability in the course of further transplantations the sarcoma alone would have been propagated.

9. As in the former transplantations of a sarcomatous tumor it was possible in these experiments to decrease and increase the virulence of the tumor experimentally.

10. The observations recorded here suggest a similar origin for the sarcomatous tumors found in mixed tumors of the thyroid in man and in different species of animals: the gland-like tumor being in both instances the primary tumor and producing a secondary sarcomatous growth in the surrounding connective tissue.

THE NUMERICAL CLASSIFICATION OF BACTERIA.

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(From the Laboratory of Hygiene, University of Pennsylvania.)

Several attempts have been made to devise a numerical system for recording the salient characters of an organism so as to facilitate the classification of the bacteria into definite groups as well as for the purpose of identifying known organisms by means of easily expressed characters. As early as 1895 (*American Public Health Association*, 1895, p. 445) Wyatt Johnston called attention to the desirability of making use of numbers to represent the characters of bacteria. He said, "It has occurred to me that all the important characteristics of a given species might be recorded more compactly than at present if a system were adopted by which the information furnished by the various tests could be represented by means of numbers, each stated in a definite order so as to form a code." Arthur I. Kendall (*Annual Report of the Massachusetts State Board of Health*, 1901, p. 415, and *American Public Health Association*, 1903, p 184) presents an attempt to utilize these suggestions of Johnston's. He makes morphology the basis for his classification along with further sub-divisions based upon cultural or biochemical features having a high percentage of constancy. Stephen De M. Gage and Earle B. Phelps (*American Public Health Association*, 1903, p. 494) also have made a contribution on the same subject. Their attention was brought to this matter by Kendall, but they followed his method only in part, as in their system "All the characters of the species are described by number, this number being derived from the combination generally of two or more allied characteristics." The group is represented by four figures, of which the first two digits signify the morphological character, the form, method of division, motility, and arrangement of flagella, according to the accepted classification of Migula.

Chester has suggested a system of numerical classification that is more comprehensive than either that of Kendall or that of Gage and Phelps. Chester makes the generic classification a fundamental part of his system and thus at once separates organisms belonging to different genera but of somewhat allied cultural characters from each other. This method, however, avoids the separation of those organisms which would be naturally grouped together by any system of classification. Chester makes the presence or absence of spores the relation of growth to oxygen and the presence or absence of liquefaction of gelatin the factors of primary importance in his system. The factors of secondary importance are the action on carbohydrates, as dextrose, lactose, and saccharose, the presence or absence of nitrite formation, and the chromogenic properties. This system, then, is based on three primary factors which are represented as a whole number and are separated from the five secondary factors by a decimal point.

Chester's key is as follows:

100.	Endospores produced.
200.	Endospores not produced.
10.	Aerobic (strict).
20.	Facultative anaerobic.
30.	Anaerobic (strict).
1.	Gelatin liquefied.
2.	Gelatin not liquefied.
0.1	Acid and gas from dextrose.
0.2	Acid without gas from dextrose.
0.3	No acid from dextrose.

0.01	Acid and gas from lactose.
0.02	Acid without gas from lactose.
0.03	No acid from lactose.
0.001	Acid and gas from saccharose.
0.002	Acid without gas from saccharose.
0.003	No acid from saccharose.
0.0001	Nitrates reduced.
0.0002	Nitrates not reduced.
0.00001	Fluorescent.
0.00002	Violet chromogens.
0.00003	Blue chromogens.
0.00004	Green chromogens.
0.00005	Yellow chromogens.
0.00006	Orange chromogens.
0.00007	Red chromogens.
0.00008	Brown chromogens.
0.00009	Chromogens.
0.00000	Non-chromogenic.

Other factors that would suggest themselves as of value in such a system are: Gram's stain, relative size of the organism, and the presence or absence of indol production. Careful study of the relative value of each of these factors shows, however, that in very few instances does either of them differentiate between organisms that are not already differentiated by the factors employed.

Chester's system has been adopted tentatively by the Society of American Bacteriologists and we have taken up the study of well-known organisms in order to classify them according to this system. (See Table I.)

TABLE I.

		Genus Bacillus.
B.	111.22210	Bacillus subtilis.
B.	111.22210	Bacillus ginglymus.
B.	111.22210	Bacillus vulgatus.
B.	111.22210	Bacillus megatherium.
B.	111.22210	Bacillus mesentericus.
B.	111.22215	Bacillus cereus.
B.	111.22217	Bacillus subtilis, var. ruber.
B.	211.11110	Bacillus cloacæ.
B.	211.11110	Bacillus vulgaris.
B.	211.11110	Bacillus mirabilis.
B.	211.22217	Bacillus prodigiosus.
B.	211.22320	Bacillus formosus.
B.	211.22225	Bacillus rheni.
B.	211.23225	Bacillus hudsonii.
B.	211.22325	Bacillus subflavus.
B.	212.11110	Bacillus coli.
B.	212.11210	Bacillus coli communis.
B.	212.11210	Bacillus paracoli (Buxton).
B.	212.11210	Bacillus paratyphosus (Cusbing).
B.	212.11310	Bacillus enteritidis (Gaertner).
B.	212.22210	Bacillus typhosus.
B.	212.21210	Bacillus dysenteriæ.
B.	212.22220	Bacillus solitarius.
B.	212.22320	Bacillus levans.
B.	212.22320	Bacillus scbafferi.
B.	212.33320	Bacillus alcaligenes.
		Genus Bacterium.
Bact.	111.22210	Bacterium mycoides.
Bact.	111.22225	Bacterium cribatum.
Bact.	211.12315	Bacterium pseudoconjunctivitidis.
Bact.	211.22216	Bacterium buccalis.
Bact.	211.23325	Bacterium fulvum.
Bact.	211.22315	Bacterium citreum.
Bact.	211.23315	Bacterium caudatum.
Bact.	212.11110	Bacterium pulmonicum (Friedländer).
Bact.	212.11110	Bacterium capsulatus (Pfeiffer).
Bact.	212.11110	Bacterium aerogenes (Escherich).
Bact.	212.22220	Bacterium pneumoniæ (Weichselbaum, Migula).
Bact.	212.22229	Bacterium czaplewskii.
Bact.	212.22310	Bacterium diphtheriæ.
Bact.	212.22310	Bacterium pseudodiphtheriticum.
Bact.	212.22320	Bacterium xerosis.
Bact.	212.23329	Bacterium rodonatum.
Bact.	212.32316	Bacterium fuscum.
Bact.	212.32325	Bacterium amabalis.
		Genus Pseudomonas.
Ps.	211.22214	Pseudomonas aeruginosa.
Ps.	211.32321	Pseudomonas fluorescens.
		Genus Micrococcus.
Mic.	211.22210	Micrococcus pyogenes, var. albus.
Mic.	211.22215	Micrococcus pyogenes, var. citreus.
Mic.	211.22216	Micrococcus pyogenes, var. aureus.
Mic.	211.22217	Micrococcus roseus.
Mic.	211.22225	Micrococcus versatilis.
Mic.	211.22228	Micrococcus fuscus.
Mic.	212.22220	Micrococcus salivarius.
Mic.	212.22220	Micrococcus catarrhalis.
Mic.	212.22220	Micrococcus fervidosus.
Mic.	212.23320	Micrococcus ovalis.
		Genus Streptococcus.
Strep.	212.22220	Streptococcus pyogenes.
Strep.	212.22220	Streptococcus pyogenes (mastitis).
Strep.	212.22220	Streptococcus pyogenes (strangles).
		Genus Sarcina.
Sar.	211.22210	Sarcina alba.
Sar.	211.22225	Sarcina lutea.
Sar.	211.22326	Sarcina aurantica.
Sar.	212.32215	Sarcina lactis.
Sar.	212.32325	Sarcina subflava.
Sar.	212.33325	Sarcina flava.
		Genus Microspira.
Mc'sp.	211.22210	Microspira schuylkilliensis.
Mc'sp.	211.22210	Microspira metschnikovi.
Mc'sp.	211.22220	Microspira finkleri.
Mc'sp.	211.22220	Microspira tyrogena.
Mc'sp.	211.22220	Microspira milleri.

A glance at the numerical formulæ of the cultures studied will show that the system is a most valuable one. It stamps certain organisms with a numerical formula that is at once distinctive and permits of easy comparison with the formulæ of other organisms.

It will be seen, however, that for other organisms the system fails to give distinctive formulæ. This is especially true for some of the spore-forming soil organisms and for some of the intestinal bacteria. In order to differentiate these closely related species it will be necessary to adopt

additional factors if any are known that positively differentiate them, or to ascertain new factors that will be o service. (See Table II.)

Table II.

B.	111.22210	Bacillus subtilis.
B.	111.22210	Bacillus ginglymus.
B.	111.22210	Bacillus vulgatus.
B.	111.22210	Bacillus megatherium.
B.	111.22210	Bacillus mesentericus.
B.	211.11110	Bacillus cloacæ.
B.	211.11110	Bacillus vulgatus.
B.	211.11110	Bacillus mirabilis.
B.	212.22210	Bacillus typhosus.
B.	212.22210	Bacillus dysenteriæ.
Bact.	212.11110	Bacterium pulmonicum (Friedländer).
Bact.	212.11110	Bacterium capsulatum (Pfeiffer).
Bact.	212.11110	Bacterium aerogenes (Escherich).
Mic.	212.22220	Micrococcus salivarius.
Mic.	212.22220	Micrococcus catarrhalis.
Mic.	212.22220	Micrococcus fervidosus.

We have attempted to utilize several of the differentiation media already in use in order to determine whether they would be of sufficient value to serve as differentiating factors. Neutral red media (agar) were employed for this purpose, but were found to be valueless. Glycerin-fuchsin-peptone solution (Andrade's medium) (*Journal of Medical Research*, 1906, vol. xiv. p. 551) was also employed and proved to be of some value, as it served to differentiate some organisms that were not differentiated by the factors employed. (See Table III.)

Our studies on the action of bacteria on carbohydrates were carried out by means of the serum-water medium of Hiss. This medium appeared to be more reliable, especially with regard to acid formation from the different sugars, than is the testing of the reaction of the contents of fermentation tubes. This fact will explain the presence of acid-producing powers for certain organisms that have been reported by others to lack this function.

We have also used this same medium containing other carbohydrates, such as maltose, dextrin, inulin, mannite, and starch, with the expectation of finding one or more of these carbohydrates of value for the differentiation of different species of bacteria. We have found, however, that, except in a few instances, these carbohydrate media were of no special value in this respect.

Although we have found this system imperfect in several particulars we consider it, however, to be of convenience in grouping bacteria, and we believe that if other important factors can be discovered it will be of service in the systematization of our knowledge of bacterial action.

Table III.

	Days.						
	1	2	3	4	5	6	7
Bacillus coli	+	+	++	+++	+++	+++	+++
Bacillus paracoli	+	+	+	++	+++	+++	+++
Bacillus X of Sternberg	+	+	++	++	+++	+++	+++
Bacillus typhosus	o	o	o	a	a	o	o
Bacillus paratyphosus	+	+	+	+	+	+	++
Bacillus dysenteriæ (Shiga)	+	+	+	o	o	o	o
Bacillus dysenteriæ (Harris)	o	+	+	o	o	o	o
Micrococcus catarrhalis	+	+	+	+	+	+	+
Micrococcus salivarius	+	+	+	+	o	o	o
Bacterium diphtheriæ	o	o	o	o	o	o	+
Bacterium pseudodiphtheriticum	o	o	o	o	o	o	o
Bacterium pseudodiphtheriticum "34"	o	o	+	+	+	+	+
Bacterium xerosis	o	o	o	o	o	o	o
Bacillus cloacæ	o	o	o	o	o	+	+
Bacillus mirabilis	a	a	a	a	o	+	+
Bacillus vulgaris	o	a	a	a	o	o	+
Microspira finkleri	+++	+++	+++	+++	+++	+++	+++
Microspira tyrogenum	o	+	+	++	+++	+++	+++
Microspira milleri	+++	+++	+++	+++	+++	+++	+++
Bacterium aerogenes	+++	+++	+++	+++	+++	+++	+++
Bacterium capsulatum	o	+	+++	+++	+++	+++	+++

+ indicates slight acidity; ++ more marked acidity; +++ marked acidity; a indicates alkalinity.

B.J.C.D

BOOK REVIEWS.

A Compend of Diseases of the Skin. By Jay F. Schamberg, A.B., M.D. Fourth edition. Revised and enlarged with 108 illustrations. Philadelphia: P. Blakiston's Son & Co., 1905.

For a quick review of dermatology Dr. Schamberg's book answers a valuable service. The compend, although small, gives a complete outline of the more usual as well as many of the rarer diseases of the skin. Several pages have been added, since the last edition, on the important subject of Roentgen and Finsen therapy; two excellent photographs show the result of the former treatment in lupus vulgaris. A few changes have been made in the text, and photographs of tinea trichophytina corporis, lupus erythematosus, and syphilis added. F. C. K.

A Text-book of Materia Medica, Therapeutics, and Pharmacology. By George F. Butler, Ph. G., M.D., Associate Professor of Therapeutics in the College of Physicians and Surgeons, Chicago. Fifth edition, thoroughly revised by Smith Ely Jelliffe, M.D., Ph.D., Professor of Pharmacognosy and Instructor in Materia Medica and Therapeutics in Columbia University (College of Physicians and Surgeons), New York. Octavo, 694 pages, illustrated. Philadelphia and London: W. B. Saunders & Co., 1906.

Not for a long time have we in reviewing a book been more impressed with its practical merits than in the case of Butler's *Materia Medica*, the fifth edition of which has just appeared. The work has been brought up to date, and adapted to the eighth revision of the *United States Pharmacopœia* by Dr. Smith Ely Jelliffe, it having been remodeled, rewritten, and reset. The size of the volume has been reduced below that of its predecessor by the use of smaller type and the omission of certain parts of the chapter on Serum Therapy. The revisor calls especial attention to the fact that the work is intended for the use of students and practitioners and not for experimental workers in pharmacology. The work has been so arranged that the drugs having a predominant action on especial systems or organs of the body are grouped together.

The first section of the book, "Pharmacology and General Therapeutics," is one which it will repay the practitioner to read. The tabulation of the "Untoward Effects of Drugs" is extremely thorough and useful. Pages 31 to 40 inclusive contain much suggestive matter, very timely in character: namely, a brief consideration of the basic principles of Arrhenius' dissociation theory as applied to therapeutics. The action of the ions of chemical compounds is one which seems to be steadily coming to the fore as a factor of recognized importance, and is one which the therapeutist can no longer afford to neglect, even though it may require a considerable rearrangement of hitherto accepted doctrines. Just how much the accuracy of therapeutics will be ncreased by these new conceptions it is impossible to say, but certainly a very large field has been opened for investigation. On the whole, the book can be unhesitatingly endorsed as a text-book upon the subject with which it deals. G. W. N.

On the Nature, Variety, and Treatment of Bodily Deformities. In a Series of Lectures by the Late E. J. Chance, F.R.C.S. Eng. With illustrations drawn on wood by the author from cases in his own practice, and many additional drawings and copious notes from cases in the editor's practice. Edited by John Poland, F.R.C.S. Eng. In two volumes. London: Smith, Elder & Co., 1905.

This is the second edition of a very interesting book first published in 1862. It is above all a scholarly study of the etiology of congenital and acquired deformities. It is given in didactic form. It is freely illustrated by line drawings made by the author, and it considers the embryology, anatomy, physiology, pathology, and mechanics of the factors that contribute to the production of deformity. The notes of the editor bring the book abreast of contemporary thought; but the student will find in the work of the author a valuable contribution to the study of orthopedics that is none the less interesting because produced at a time when this specialty had to fight for recognition of its right to existence, as shown in the controversy contained in the introduction.

The suggestions on treatment are too general and scant to make the treatise serviceable in this regard as a book of reference, but the student of the etiology of deformity will be well repaid for reading this logically and graphically presented consideration of the causes of deformity. The publishers' work is creditable. J. M. S.

A Laboratory Guide in Bacteriology. By Paul G. Heinemann, Sc.B., Fellow in Bacteriology, University of Chicago. The University of Chicago Press, 1905.

Dr. Heinemann presents in this book the outline of his course in bacteriology at Chicago. He aims to set clearly before the student the way to do things, and most of all to impress upon him why every step is taken, sometimes a difficult task, but one which the author leads up to in a simple but very scientific manner. The *Guide*, moreover, supplies to the teacher of such a course a system, simple but sufficiently comprehensive, to lay the foundation of intelligent interpretation of clinical pathological reports, or of subsequent research work in bacteriology or pathology. The worker is not flooded with facts but is encouraged to read the standard books and magazine articles, references to which are given freely in the text. Particular attention is given to technique, more than one m thod being sometimes given, but the simplest always emphasized. The book will prove to be a great help to the teacher or student of a course in bacteriology. H. F.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

A CLINICAL STUDY OF GASTROPTOSIS, WITH SPECIAL REFERENCE TO THE VALUE OF THE BISMUTH SKIAGRAPH SHADOW IN DETERMINING THE TOPOGRAPHY OF THE GASTROINTESTINAL TRACT.

By Charles B. Worden, A.B., M.D.,
Associate in Diseases of the Stomach and Intestines, Philadelphia Polyclinic Hospital.

Discussion by Joseph Sailer, M.D.,
Professor of Diseases of the Stomach and Intestines, Philadelphia Polyclinic Hospital; Associate in Medicine, University of Pennsylvania,

Henry K. Pancoast, M.D.,
Skiagrapher to the University Hospital,

and

Gwilym G. Davis, M.D., M.R.C.S. (Eng.),
Associate Professor of Applied Anatomy, University of Pennsylvania.

REMARKS BY DR. CHARLES B. WORDEN.

The following report is based upon the study of forty cases presenting gastric or gastrointestinal symptoms. This work is reported from the clinic for diseases of the stomach and intestines at the Polyclinic Hospital, service of Dr. Sailer. The cases were taken from various sources. Thirteen were private cases of Dr. Sailer's, ten of Dr. Musser's, two of the writer's, five from Dr. Sailer's clinic at the Polyclinic Hospital, nine from the wards of the University Hospital, and one from the writer's clinic at the Presbyterian Hospital. In the study of these cases particular stress has been laid upon outlining the stomach and in obtaining its size, shape, and position. To do this the following methods were used: Inspection, percussion, auscultatory percussion, auscultation with the tuning-fork, inflation with carbonic acid gas or air, illumination by the electrodiaphane with the aid of fluorescent solutions, and the use of skiagraphs. After the ordinary methods of physical examination had been employed *x*-ray pictures were taken in each case by Dr. Henry K. Pancoast. The technique used in taking the pictures was as follows: Bismuth subnitrate held in suspension in mucilage of acacia was either poured into the stomach through the stomach tube or was swallowed by the patient; the latter method was principally used. The bulk of the bismuth acacia mixture varied from six to thirty-two ounces; the amount of bismuth varied from one to four ounces. Immediately after the bismuth had reached the stomach the pictures were taken, the patient being in the standing position, and the plate in contact with the anterior abdominal wall. The *x*-rays were thrown posteriorly, the patient holding the breath during full inspiration for an exposure of eight to fifteen seconds. The exposures were made with the breath held, thus eliminating blurring by respiratory and peristaltic movements. After the picture has been taken it is advisable to siphon the bismuth mixture out of the stomach. In several cases as much as four ounces of bismuth was left in the stomach, with no unpleasant symptoms; but on the other hand six cases showed toxic symptoms after this amount had been left in. For the purpose of obtaining the lower border and segment of the stomach six ounces of the emulsion containing one ounce of bismuth is sufficient. This amount has been left in the stomach, with no bad effects.

Comparison of the Results Obtained by Skiagraphs with Results Obtained by Other Methods.

Examination shows that by this method the stomach and intestines can be studied more completely and more accurately than has heretofore been possible. In some cases skiagraphs have shown marked prolapse which repeated physical examinations failed to indicate. The difficulties encountered in inflation, illumination, etc., that is the confusion between the tympanitic note over the stomach and that over the colon, the tendency in distending a stomach with gas or air to push before it a distended colon, making the distinction between the two less marked, also the difficulties presented by the fact that the undistended stomach is not in contact with the abdominal wall and when empty is contracted high up under the diaphragm and almost inaccessible to physical examination, are not met with in examinations by skiagraphs. The conditions under which skiagraphs are taken are approximately constant, the bulk and weight of the

stomach contents and the distention of the stomach being known. The results from skiagraphs are not only more accurate but are by far more exhaustive in the information obtained.

The œsophagus can be studied for stricture, dilatation, or sacculation; the cardia for stricture, and the size, shape, position, and the smoothness of its wall determined.

A complete study of the body of the stomach can be made, and of great importance is the clearness with which the upper curvature and the pylorus is shown in the skiagraphs. Regularity of the stomach wall can be observed and variations from the normal noted. In Case 7 it was possible to diagnose a tumor invading the stomach wall by the irregularities of the lower border.

The knowledge obtained of the shape of the stomach and the position of the pylorus are two important points made possible by skiagraphs. The establishment of these points by ordinary methods of examination is uncertain and often impossible. Mechanical difficulties in stomach drainage can be recognized especially in cases of prolapsus when the stomach bends sharply on itself.

In the examination of the skiagraphs of forty cases the following points were particularly noted: The size, shape, and position of the stomach, the position of the pylorus, and the position and size of the colon.

Case.	Gastroptosis.	Dilatation.	Low pylorus.	Kinking.	Prolapse of colon.
1	+		+	0	
2	+		+	0	×
3	+		+	0	+
4	+	0	0	+	\
5	+		+	+	×
6	+		+	+	×
7	0		0	0	
8	0	0	0	0	
9	+	+	+	0	+
10	+	+	+	+	×
11	+		+	+	×
12	+	+	+	0	·
13	+	+	+	0	×
14	+	0	0	0	+
15	+	+	+	0	+
16	+	+	+	0	×
17	+		+	0	×
18	+	+	+	0	×
19	·	0	+	0	·
20	+		+	+	×
21	+		+	+	×
22	+	+	+	0	·
23	+	·	·	0	·
24	+	·	·	+	×
25	+	+	+	+	×
26	·	+	+	0	·
27	·	+	+	·	×
28	0	0	0	0	+
29	+	+	+	·	×
30	·	+	+	+	·
31	+	+	+	+	×
32	+	+	+	0	×
33	+	+	+	+	×
34	+	+	0	+	+
35	0	0	0	0	+
36	0	0	0	0	0
37	+	+	0	0	·
38	0	·	0	0	+
39	0	0	0	0	·
40	0	0	0	0	×

× = colon not examined.

Gastroptosis. Analyzing the results of skiagraphs of these forty cases the first significant fact is that thirty-one show the presence of gastroptosis.

In some of these cases gastroptosis was suspected before skiagraphs were taken, by the presence of such symptoms as a relaxed abdomen, with separation of the recti muscles, or by the results of inflation, the use of the gastrodiaphane and the ordinary methods of physical examination. On the other hand, skiagraphs showed the presence of prolapse of the stomach in cases in which repeated physical examinations failed to indicate it. Schüle confirms this statement (*Archiv f. Verdauungs Krank.*, December, 1905, xi. p. 509). The subjective symptoms often threw but little light upon the presence of prolapse and were often entirely at variance with the findings. The subjective symptoms found were, in general, symptoms of impaired motility, of failing nutrition and nervous disorders, and they seldom corresponded to conditions made evident by the skiagraphs. One extreme case of prolapse presented no gastric symptoms whatever, and the skiagraph was taken as a matter of interest on account of a wide diastasis of the recti. The strength of the gastric musculature, the favorable shape of the stomach and position of the pylorus evidently accounted for the compensation in this case.

In the most extreme case (19) of prolapse, the stomach extending to the pelvis, with the exception of loss of appetite, no gastric or intestinal symptoms were present. Failing nutrition and intense nervous symptoms led to the *x*-ray examination, physical examination having failed to show the true position of the stomach. At present writing gastric symptoms are coming on rapidly: fermentative emesis and retention making sufficient feeding impossible, operation was advised.

The degree of ptosis varied from cases in which the lower border of the stomach reached the umbilicus to cases in which the descent of the body of the stomach was complete.

The value of the knowledge of the position of the stomach is greatly augmented by the exact information as to its size and shape and as to the position of the pylorus; it is in ascertaining these points that the value of the skiagraphs is most evident.

Dilatation. In twenty-nine of the forty cases examined some degree of dilatation was seen. In two cases dilatation was found with no prolapse and in only two cases was prolapse found without some degree of dilatation. The conditions which relax the gastric attachments would seem to relax the gastric wall also.

The first eight to nine inches of the duodenum are firmly attached to the spine (see discussion by Davis), and the cardia is also a fixed point. The stretching of the gastrohepatic ligament allows the stomach to drop from these more or less fixed points, and the weakening and stretching of the gastric wall would seem to follow prolapse.

Shape of the Stomach. The shape of the stomach from a study of skiagraphs is shown to be most variable. It varies from a pear-shaped organ lying in a partly horizontal axis to a long stretched-out cylindrical organ lying almost in the perpendicular, with a pouch-like formation at the lowest point or to a J-shaped organ, with the upper extremity at the cardia and the lower extremity at the pylorus, its general axis being vertical. It is believed that the shape of the organ is skiagraphed under natural conditions, since the weight and bulk of the bismuth mixture are not more than that of the ordinary meal. A patient assumes a natural position, *i. e.*, standing, and is free from the effect of tight clothing. Although pictures are taken during full inspiration it is not forced inspiration, and it is not believed that the full inspiration affects the position of the stomach to any appreciable extent. Holznecht and Brauner, in a recent article, in watching the stomach by the fluoroscope, claim that the stomach moves downward four fingers' breadth and changes in shape during forced inspiration. Dr. Pancoast took two pictures of the same case, one during forced inspiration and one during forced expiration, and found the difference in the position of the stomach of but little moment, the actual difference being about three-sixteenths of an inch and with but slight change in shape. In the study of the shapes of these stomachs one point seems of particular significance. The cases of gastroptosis show sometimes a low position of the body of the stomach and an acute angle as the stomach sharply bends to reach the higher pylorus; this forms what I shall term as kinking in the pars pylorici; this is particularly noticeable in the perpendicular tubular stomach. The stomach can also be seen bending *on itself* so sharply it is difficult to distinguish the two sections of the stomach. (See Plates I., II., and III.) This shape of the stomach seems to have an important bearing on the condition of motility, and may explain why in some cases of marked prolapse motility remains fairly good, while in others of less ptosis, but with this angular distortion, motility is so much embarrassed. Of the forty cases reported fifteen showed the presence of kinking in the pyloric region; to bring this out it is advisable to use one quart of the bismuth emulsion, for by using this quantity the upper curvature and the pylorus are shown very clearly.

Position of the Pylorus. The pylorus in the great majority of cases lies to the right of the median line; in five cases it was found on the left of the median line. This was most marked in the cases of the tubular shaped stomach lying almost in the perpendicular; the pylorus in general was found prolapsed. This was shown only by the *x*-ray pictures, as illumination and inflation gave very unsatisfactory results in locating this point; by using the larger amount of bismuth the pylorus can be accurately located, the contour, direction, and smoothness of its walls noted. Of the thirty-two cases showing gastroptosis twenty-eight showed a low pylorus; in most of these cases it occupied a position just to the right and below the level of the umbilicus.

Prolapse of the Colon. This condition has been found difficult to diagnose without the aid of the radiograph; of nine cases in which the colon was examined by this means eight showed prolapse. To picture the colon the method is used which was reported by the writer to the Medical Section of the College of Physicians of Philadelphia in April, 1904; two ounces of bismuth in eight ounces of milk or acacia is injected into the rectum after the intestine has been thoroughly emptied. Exposures were made fifteen to forty-five minutes after the introduction of the bismuth. These pictures are of interest as showing the rapidity of antiperistalsis, which must account for the ascent of the bismuth mixture as far as the ileocæcal valve in fifteen minutes. In two cases examined for stricture the ascent of the bismuth stopped at the point of obstruction and was of diagnostic value in locating the lesion. By giving bismuth by mouth and at the same time introducing it by rectum satisfactory evidence can be obtained of the relative position of the stomach and colon as well as their respective size and shape. To show the small intestine pictures taken twelve to fifteen hours after the bismuth is given by mouth would be of use in locating stricture or obstruction. The cæcum is always found filled; the transverse colon can easily be seen and is seldom found placed horizontally; it passes from right to left in an upward direction in a curve, with the convexity downward; the splenic flexure usually is high up close to the diaphragm; in one case it was found deep in the pelvis. The splenic flexure frequently forms an acute angle and may be doubled on itself; the hepatic flexure is found usually lower than the splenic flexure; this also often forms an acute angle and is doubled on itself. Gas collections are usually seen at both flexures. The chief points to be noted in the study of the intestines are the low position of the hepatic flexure and the high position of the splenic flexure; the acute angles at these flexures, and the fact that intestinal contents seem to remain longer in the cæcum than at any other point.

Some Results in the Treatment of Gastroptosis. The treatment in general has consisted in hygiene, diet, drugs, lavage, electricity, rest, massage, abdominal belts, and operation. In the extreme cases of gastroptosis to secure proper drainage abdominal support or surgical treatment are necessary, the results from the use of belts or abdominal supports have been in some cases gratifying; eight cases have shown marked relief from symptoms by this means. In Case 5, extreme prolapse, with dilatation, low pylorus, and kinking at the pyloric portion, an abdominal support of adhesive plaster consisting of long strips of plaster passing from below the stomach in a curved line upward and outward, passing

across the abdomen and posterior thorax to a point between the scapulæ, overlapping each other on each side respectively, relieved the symptoms of poor motility.

A picture taken with this support on shows the stomach little if any elevated; the support evidently has altered the shape of the stomach enough to allow better drainage from the pylorus. Five cases have been operated upon: three have had gastroenterostomy performed, one gastrofixation, and one gastrofixation and colonfixation. Case 22 appeared at my clinic at the Presbyterian Hospital, May 15, 1905; has been practically incapacitated for ten years. Chief symptoms: pain, pyrosis, nausea, vomiting, flatulence, constipation, headache, and extreme nervousness. The stomach was found so prolapsed she was sent to the Woman's Medical Ward under Dr. Stryker and Dr. Hughes, and later to Dr. Willard. Operation of gastrofixation was performed by Dr. E. B. Hodge, in October, 1905, in the service of Dr. Willard; shortening of the gastrohepatic ligament, with the addition of a fold taken in the anterior wall of the stomach, was performed. The result in this case has been a relief of symptoms and gain of thirty pounds; the patient is now upon a liberal diet.

Some Cases in Which Skiagraphs were of Service in Making the Diagnosis Often when the Diagnosis was Impossible by Other Means of Physical Diagnosis.

Miss M. H. (case of writer's), aged twenty-two years; family history negative; personal history negative, with exception of typhoid fever nine years ago. Has had stomach trouble for fourteen years. Chief symptoms have been fulness and distress after eating, constipation, headache, nervousness, acne, appetite poor and irregular.

PLATE I.

PLATE II.

PLATE I.—Shows gastroptosis, dilatation, saeculation, and kinking of the pyloric part of the stomach.
PLATE II.—Shows cylindrical shape of the body of the stomach, marked kinking of the pyloric region.

Test-meal, Ewald, t. a. 60. Free HCl, 20. Much mucus present. Retention.

Skiagraph showed some degree of gastroptosis.

An abdominal belt was applied, which has greatly benefited gastric motility. Persistent lavage is gradually reducing the great quantities of mucus secreted.

Miss L. B. S. (case of Dr. Sailer's), aged twenty-seven years, nurse. Attacks of nausea, distention of the abdomen, at rare intervals vomiting, chronic constipation, pain after eating, pain through abdomen coming on immediately to one hour after meals, sour eructations, intestinal mucus. Test-meal, total

acidity, 44. The liver extends two inches below costal border, right kidney is palpable, gastric tympany, sixth rib to one-half inch above umbilicus and from median line to the anterior axillary line. Tuning-fork gives some outlines, tenth rib attached, no separation of recti, left kidney not palpable, on deep inspiration spleen extends to one inch of the costal border, peristalsis diminished.

Skiagraph showed marked gastroptosis. Abdominal support gave great relief.

J. E. S. (case from the Stomach Clinic at the Polyclinic Hospital), single, aged twenty-four years. Began at the age of sixteen years to have heartburn, water-brash, vomiting, eructations, soreness in epigastrium. At present appetite is good, regurgitation of food, pyrosis, pain, constipation, drowsiness after meals, bad taste in the mouth, fulness, and distress. Test-meal, Ewald, fifty minutes, t. a. 66, free acid 18, retention; second test-meal, Ewald, one hour, t. a. 60, free acid 30. Stomach inflated and diaphane used. Diagnosis was not complete without the aid of a skiagraph, which showed marked degree of gastroptosis.

Miss M. L. (case from the Stomach Clinic at the Polyclinic Hospital), aged fifty-one years, milliner, attacks of indigestion lasting for weeks at a time; these attacks started while in India upon a very irregular diet, costive, appetite irregular, eructations, pyrosis, pain, thirst abnormal, fulness and distress after meals, headache. Skiagraph showed marked degree of gastroptosis. Very much improved by belt.

Mrs. Y. K. (case from the Stomach Clinic at Polyclinic Hospital), aged twenty-eight years, housewife. For the past ten months continued pain in epigastrium, worse after eating, appetite good but has sitophobia, difficulty in swallowing, nausea, pyrosis, constipation, pasty taste in mouth, fulness and distress marked, headache, palpitation, inflation with carbonic gas and air shows gastroptosis, fine peristaltic wave is seen when the stomach is inflated, passes from left to right. Skiagraph showed marked degree of gastroptosis. Abdominal belt gave some relief. Operation advised.

S. R. (case from the Stomach Clinic at the Polyclinic Hospital), aged forty years, married, white. Began one and a half years ago with pain in the stomach; was treated at the Pennsylvania Hospital for vomiting and pain in epigastrium, and an exploratory operation was performed. Progressive

PLATE III.

PLATE IV.

PLATE III.—Shows gastroptosis, dilatation, and kinking of the pyloric part of the stomach.

PLATE IV.—Shows the outline of the stomach in connection with ptosis of the transverse colon, high position of the splenic flexure and adhesions between the transverse and descending colon.

loss of weight, vomiting, pain and heaviness in the stomach, bowel movements from five to six daily, no appetite, very weak, present weight 116, former weight 160; test-meal, egg albumen, white of one egg in a pint of water, forty-five minutes, t. a. 26, free acid 14. Numerous test-meals were given showing a general subacidity with much mucus; *x*-ray picture shows the stomach in position with the colon "M" shaped. (See Plate V.) One year after treatment: test-meal, Ewald, one hour, t. a. 36, free acid 26, weight 117; haemoglobin, 80 per cent.; red blood corpuscles, 3,900,000; white blood corpuscles, 6000; stomach was frequently dilated with sour; constipated; no localized pain; average weight 115, at present 96. Physical examination: Tenth rib is not attached, separation of recti, upper liver dulness at sixth rib, stomach tympany starts at sixth rib, the lower border of the liver extends to the level of the umbilicus, the right border as far as the parasternal line, the lower border of the right kidney extends to the level of the umbilicus, left kidney and spleen not palpable; a nodule is felt an inch and a half from the anterior superior spine of the ilium in a line between the umbilicus and the right anterior superior spine; the outline of the stomach can be seen; greater curvature

PLATE V.

PLATE VI.

PLATE V.—Shows prolapse of the transverse colon.
PLATE VI.—Shows ptosis of the sigmoid.

carbonic gas; the gastrodiaphane was frequently used. An operation for inguinal hernia was performed at the University Hospital, since which time patient has gained eighteen pounds.

Miss M. H. (case of Dr. Sailer's), aged fifty years, schoolteacher, family history negative; past history: delicate, slender, never strong but energetic; three years ago became excited and had sense of something giving way in abdomen; has never recovered health since; at varying intervals after meals has oppression and distention, which is relieved by eructations of flatus or vomiting, the quantity vomited varying from a pint to one quart; the vomitus is bitter and being an inch and a half above the symphysis pubis, lesser curvature apparently at the level of the umbilicus extends to the right two inches to the right of the median line; loud splashing, tuning-fork confirms percussion; there is apparent obstruction at the pylorus, pressure upon the stomach at first causes no sound and then a sudden gushing; distinct peristaltic contractions in the gastric area may be seen passing from left to right and from above downward; the gastrodiaphane was used with a fluorescent solution; the light showed very clearly through the abdominal wall and followed a line from the anterior superior spine to the symphysis on both sides; the position of the lesser curvature could not

be determined. Skiagraph confirms diagnosis of gastroptosis.

C. M. F. (case of Dr. Sailer's), aged forty-five years, family history negative, except family is prone to weak stomachs. Past history: appendicitis at thirty-three, cystitis at forty-one, alcohol to excess up to one year ago, tobacco, five to six strong cigars a day, began to have stomach trouble some years ago, for the past four or five years has had diarrhœa after eating, was obliged to live on kumiss, food caused sour eructations, stools contain masses of undigested food, little nausea , voluntary vomiting, costive, soreness in epigastrium, especially after exposure to cold. Test-meal, Ewald, fifty-five minutes, much mucus, t. a. 83, free acid 47; second test-meal, sixty minutes, t. a. 84, free acid 40; given lavage with protargol. Skiagraph showed gastroptosis and dilatation.

Mrs. J. W. F. (case of Dr. Sailer's), past history: Past nine months has had indigestion at varying periods, a few minutes to four or five hours after eating there is discomfort, relieved by vomiting; vomit sour, "sets teeth on edge;" no pain in abdomen, increasing nausea relieved by vomiting; dull, diffuse headache; insomnia, constipation; blood hæmoglobin, 75 per cent.; red blood corpuscles, 4,770,000. Test-meal, Ewald, t. a. 70; test-meal, Fisher, t. a. 130; liver at the sixth rib, lower border, not palpable; kidneys not palpable, peristalsis active, tenderness over epigastrium. Skiagraph shows gastroptosis of marked degree. (See Plate III.) Abdominal belt gave great relief.

Miss M. C. (case of Dr. J. H. W. Rhein). Two years ago pain behind the sternum associated with hiccough, costive, difficulty in swallowing, nausea when eating, vomits during meal-time, very sour acid eructations, discomfort in abdomen, appetite poor, both tenth ribs unattached, no separation of recti, kidneys and spleen not palpable; no tympany over gastric region, intragastric pressure very high. With the diaphane the light is seen at the umbilicus. Skiagraph showed marked gastroptosis. This patient was operated upon and gastroenterostomy performed by Dr. B. C. Hirst, with good result.

Dr. M. (case of Dr. Sailer's), aged fifty-three years, neuropathic hereditary; for the past twenty years has had stomach trouble; started with pain in the epigastrium, usually some time after eating; dull, worrying pain lasting an hour or more, at present almost continually; immediately after eating there is oppressive pain and weakness lasting for hours, distinct increase about two hours after eating; no nausea or vomiting, costive, appetite is poor, no headache, insomnia due to pain; the diaphane shows a light just below and just to the right of the umbilicus; the liver at the level of the umbilicus, gastric tympany sixth rib posterior axillary line to one inch below costal border; test-meal, Ewald, one hour, t. a. 64, mucus, free acid present. Operation was advised as the skiagraph showed extreme degree of gastroptosis and dilatation.

Mr. M. W. C. (case of Dr. Sailer's), aged thirty-three years, teacher, single; insomnia, poor appetite, costive, pain in epigastrium, eructations three hours after eating relieved by hot drinks, abdomen tender, nausea, no vomiting; pain after eating is relieved by out-door life and work, made worse by anxiety, worry, fatigue; gastric tympany, seventh rib in middavicular line descending as far as the umbilicus, slight separation of recti; test-meal, Ewald, fifty minutes, t. a. 40, mucus present; hæmoglobin, 70 per cent.; red blood corpuscles, 5,500,000. Skiagraph showed marked degree of gastroptosis.

Mrs. C. B. (case of writer's), aged twenty-eight years. Family history: neurotic. Personal history: has one child aged three years; has always been extremely nervous. Absence of appetite, loss of weight, vomiting, melancholia. Skiagraph showed the lower border of the stomach reached as far down as the pelvis and that the body of the stomach was kinked. Dr. Beyea operated July 17, 1906, replacing the stomach and relieving the kinking by shortening the gastrohepatic ligament. At the present writing she is making a good recovery.

Holznecht and Brauner (*Wien. klin. Rundschau*, 1905, xix.) consider the fluoroscope of more service than the radiograph; by the fluoroscope they can test palpatory and respiratory motility of the stomach. They state that on deep inspiration the stomach moves downward four fingers' breadth and changes in shape, becoming longer and narrower. They give 10 grams of bismuth in 50 grams of water and note the deepest part of the stomach; they note also the influence of deep massage in pressing the stomach down and also the influence of respiratory movements. They consider this method of great value in diagnosis of carcinoma and hour-glass stomach, as well as dilatation and gastroptosis.

Hulst (*The Physician and Surgeon*, September, 1905) goes farther than other investigators in the technique of exposures, eliminating blurring caused by respiration and peristalsis. He reports twenty-two cases. He used bismuth nitrate suspended in one quart of milk and taken slowly, with or without bread. He takes one skiagraph immediately after eating; he takes a second skiagraph six hours after the bismuth meal, allowing no food in the meantime; he takes a third skiagraph twelve to fourteen hours after the meal, as the best time for pictures of the colon. He has not used bismuth enemata because he has had satisfactory results by giving the bismuth by the mouth.

Hulst's *x*-ray pictures show the stomach and colon differently from descriptions in the majority of text-books. The current conception of the size, shape, and position of the normal stomach must be modified; to get a correct idea of displacement the pictures must be taken standing; the first

skiagraph shows the size, shape, and position of the stomach, the second shows the motility of the stomach, and the third shows the position, size, and shape of the stomach.

Pfahler (*Archiv. of Phys. Ther.*, July, 1905) used one ounce of bismuth in twenty ounces of milk. He regards this method as a method which is accurate, which gives permanent records, and is of no danger, causes no pain or inconvenience to the patient. He takes pictures in the prone position and standing, immediately after the bismuth has been given, then at intervals of six, twelve, and forty-eight hours.

Rieder (*Fort. auf. dem. Gebeit. der Roentgenstr.*, February, 1905) says that all other methods of outlining the stomach are replaced by the radiograph. He says that an *x*-ray picture of the empty stomach is deceptive on account of the contractility of the stomach. He disapproves of inflating with carbonic gas on account of danger to the patient. In his series of radiographs the pylorus is easily seen; the duodenum is not easily seen, as it is covered by the liver and stomach. The jejunum in its upper part is not clearly seen, the lower part together with the ileum can be easily made out. The small intestine is less readily seen on account of active peristalsis, the chyme is more diluted, the walls are smoother and prevent the bismuth chyme from settling there. The termination of the small intestine at the cæcum can be seen, also the valve; the large intestine can be recognized by the plicæ semilunares; the termination of the cæcum into the ascending colon can be recognized. The hepatic flexure, the transverse colon, the splenic flexure, and the descending colon can easily be seen. Still better results can be obtained from the use of bismuth enemata; he says that bismuth does not show gastric motility, but does show intestinal motility. Chyme stays longest in the cæcum and the ascending colon. These portions of the intestine may be full while other portions are empty. He states that this may have some bearing upon the causation of appendicitis.

Tousey (*New York Med. Journ.*, May 21, 1904) prefers fluoroscopic work. He also uses radioactive and fluorescent solutions as an assistance in *x*-ray work.

Dalton and Reid (*Lancet*, April 1, 1905) obtain the position of the stomach by the *x*-rays by using an œsophageal tube filled with bismuth. They use both the fluoroscope and radiograph. They state in conclusion that this method certainly enables a physician to recommend an operation with the greatest confidence.

Schule (*Archiv f. Verdauungs Krank.*, December, 1905) compares the accuracy of mapping out the stomach by percussion, inflation, etc., to the results obtained by use of *x*-rays. He considers the latter method of the greatest value and enumerates the sources of error which are avoided by this method. He refers particularly to the confusion caused by the transverse colon when it lies in front of the stomach. When the stomach is artificially distended the transverse colon is pushed ahead of it against the abdominal wall, making it almost impossible to distinguish the two by the ordinary methods.

Rieder (*Münch. med. Woch.*, 1906, iii.) gives extensive results in the use of the fluoroscope by watching the course of bismuth throughout the course of the digestive tract. His pictures illustrate also the motor function of stomach and intestines. The pylorus is noticed to be the motor orifice of the stomach; it opens and shuts rhythmically, stopping when the small intestine becomes filled up; thus is prevented too great filling. Bismuth subnitrate neither increases nor decreases the activity of the stomach, and its digestive power can thus be readily determined. The fluoroscope shows that the stomach contents diminish gradually; fluids are emptied quicker than solids, and large quantities incite greater motility than small quantities; the stomach works quickest at the beginning of digestion. A small amount of food stays in the deepest part of the stomach a long time.

Conclusions. *x*-ray pictures of the stomach and intestines for diagnostic purposes excel by far any other method. To the surgeon, skiagraphs of these organs are of the greatest value and operations upon the digestive tract for prolapse, etc., can be undertaken with far more confidence. The permanency of the record secured by skiagraphs and the accurate manner by which the position of the stomach and intestines can be ascertained before, during, and after treatment add to the value of the method.

Skiagraphs have proved of value in the diagnosis of stricture, dilatation, and sacculation of the œsophagus; of dilatation, prolapse, hour-glass stomach, and cancer of the stomach; of stricture, dilatation, and tumors of the intestine; of prolapse of the colon and sigmoid.

In addition to the accuracy of the results obtained the simplicity of the technique, provided a good *x*-ray apparatus is accessible, and the comparative comfort to the patient are to be mentioned; the inconvenience being no more than that caused by the passage of the stomach tube. Siphoning the bismuth mixture from the stomach excludes the element of danger to the patient, a distinct advantage over inflation.

The present work was begun two and a half years ago, and the present method used is the result of gradual development.

It was begun by taking a series of pictures of the intestine, which was reported to the Medical Section of the College of Physicians in April, 1904. It followed the line of work suggested by Cannon in his work upon guinea-pigs, mice, and dogs. The work has been done in connection with my service at the Polyclinic Hospital, in the clinic for diseases of the stomach and intestines, in the service of Dr. Sailer, and I wish to acknowledge his kind co-operation and

assistance, and also to thank Dr. H. K. Pancoast for his skilful work in the *x*-ray laboratory of the University of Pennsylvania.

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REMARKS BY DR. JOSEPH SAILER.

Since Glenard first called attention to the displacement of abdominal viscera, and suggested that it was a possible physical basis for the condition called neurasthenia, the subject has been studied with more or less interest, curiously enough, not always by the medical profession as a whole, but certain individuals have been impressed by the importance of this condition, often paying attention only to the displacement of a single organ, as for example, the interest that was excited by the ptosis of the kidney a few years ago

The diagnosis of gastroptosis is by no means easy. I say this from what I believe is a reasonably full experience. There is not a method upon which we can with certainty rely if it be not the *x*-ray. Percussion, inflation, the gastrodiaphane have all led me into error, although I believe that the repeated employment of inflation with the tube is a reasonably certain procedure. This, however, is not altogether an agreeable method to the patient—often indeed it is associated with actual discomfort—and it gives information only regarding the lowest point and the furthest point to the right.

The gastrodiaphane when it works is almost ideal. The bright point of light following the greater curvature, and slipping into the pyloric end of the stomach, where it stops, is so clear and characteristic that there is no further doubt regarding the position of the organ. Unfortunately, even when solutions of fluorescin are employed the results are by no means constant, and it is often impossible to see the light or, if it is seen, to get it to move in the desired direction.

To my mind the examination of the stomach by means of the *x*-ray is greatly superior to all other methods for the following reasons: It is speedy, it is precise, and it gives a variety of information that cannot be obtained by any other method. It is true that sometimes the pictures are indistinct and unsatisfactory, so that the results cannot be regarded as sufficient in every instance; but in at least 90 per cent. of those of my cases in which Dr. Pancoast employed it during the past winter the results were practically perfect.

When I speak of the variety of information that is obtained by the use of the *x*-ray I refer not merely to the outline of the greater curvature of the stomach, but also to the distinct outline of the lesser curvature and its character and peculiarities. Moreover, in the majority of cases the position of the pylorus is indicated as sharply and clearly upon the plate as the position of the greater curvature. It shows as a transverse dark line between the shadows of bismuth suspension in the stomach and of the small portion which has already penetrated into the duodenum. The importance of a clear knowledge of the condition of the lesser curvature I believe has not hitherto been properly appreciated, but in not one of the cases in which the lesser curvature was folded back upon itself with a sharp bend about the middle was there a failure of retention. And in the cases in which there was hypermotility it could very clearly be seen that the lesser curvature appeared as a continuous curved line. The obvious conclusion is that in those cases of gastroptosis with retention of gastric contents (and I believe that this retention is probably the most serious result of the ptosis) our object should be if possible to eliminate this kink, and I am rather inclined to believe that various operations that have been done upon gastroptosis with considerable success act less by actually elevating the stomach than by straightening the lesser curvature. This is particularly true, I think, of the operation performed by Dr. Beyea. Gastroenterostomy, on the other hand, without measures designed to relieve the kinking, can only be regarded as a makeshift.

But the information yielded by these *x*-ray pictures regarding many other organs within the abdomen is considerable. Not infrequently the spleen can be seen causing a distinct depression in the fundus of the stomach. It seems unlikely, however, that such a depression could interfere in any way with the motility of the organ. The position of the duodenum can rarely be traced for more than an inch or two. On the other hand, the position of the splenic and hepatic flexures is usually easily made out on account of the presence of a bubble of air which shows upon the print as a clear area usually traversed by lines representing the folds in the colon. Often the position of the transverse colon can also be distinctly observed.

It is worth while, I think, to note in passing that the original contention of Glenard that in cases of splanchnop-

tosis the hepatic flexure of the colon is lower than the splenic flexure of the colon, seems to be almost invariably true. Glenard, of course, regarded the descent of the hepatic flexure as the most important element in splanchnoptosis, and probably the primary one to which all the others were due. Nowadays we are more inclined to look upon the condition as, in the majority of cases, entirely congenital, no one organ or group of organs being more implicated than the others.

The value of the routine examination of the stomach, as an indication for treatment, cannot I think be overestimated. To instance a few of my cases: Miss G. was muscular, well-developed, with a short trunk and exceptionally broad hips, in whom inflation and percussion had failed to suggest displacement of the stomach; but the discovery of an extreme degree of gastroptosis, followed by the application of a satisfactory binder, produced almost immeditate relief. Mrs. F was a tall, powerfully built young woman who had been quite athletic, but who in the last year had emaciated very rapidly. The radiogram indicated that the greater curvature of the stomach was very near the symphysis, that the lesser curvature was sharply bent, and that the pylorus was just to the right of the umbilicus. An efficient binder caused a gain in weight which for several weeks averaged a pound a day.

The *x*-ray method is also of value in studying the results of treatment. In one patient, upon whom gastroenterostomy had been performed by Dr. Martin for stenosis of the pylorus, it was easy to see that the abnormal opening was acting splendidly, the bismuth passing readily into the small intestine at that point.

This method has hitherto proved less satisfactory in stout than in thin persons. Otherwise, aside from the defects in the apparatus or plates, it presents no difficulties. It is not, however, without certain dangers. Several cases have exhibited the symptoms of poisoning which have been so similar that we have been led to assume a common cause. Four such cases have been under my observation, and two of them were severe.

Miss M. received two ounces of bismuth in suspension about 4 P.M. About 5 A.M. the following morning she awoke in great distress with dyspnœa. She felt very weak, and had distinctly the fear of impending death. I saw her about 7.30 P.M., and at that time the symptoms had, according to her mother and sisters, not altered perceptibly. She was deeply cyanosed; the respirations were between 30 and 40 per minute; the pulse was full and bounding; the heart's action could easily be felt through the clothing; and there was still profound weakness and fear of death. In addition the patient complained of slight nausea. Upon careful inspection the cyanosis had a distinct ruddy tinge similar to that seen in cases of polycythæmia. Unfortunately it was impossible at that time to make a blood count. The patient was given hot coffee by the mouth and strychnine and morphine hypodermically. The coffee was almost immediately vomited and the patient felt relieved. In a short time she became sleepy, and in the course of the afternoon had almost entirely recovered, although as a matter of precaution I kept her in bed for several days.

Mrs. P. received between two and three ounces of bismuth in suspension at 11 A.M. About 10 P.M. her symptoms became alarming, and Dr. Johnson, of Chestnut Hill, was called to see her at my suggestion, after a consultation over the phone. He described the symptoms as essentially the same as those in the previous case: cyanosis, the fear of death, rapid respirations, weakness, dyspnœa on slight exertion, and nausea. Coffee was administered, causing her to vomit with some relief. The symptoms gradually abated, and when I saw her about 1 P.M. the following day she had practically recovered.

After excluding antimony and arsenic we were at a loss to account for this poisoning, until a physician who is a patient of mine suggested the analogy of the symptoms to excessive doses of nitrites. It seems very likely that this is the explanation, for Werner (*Münchener med. Woch.*, January, 1906) has recently shown that trypsin is activated by the *x*-rays, and it is altogether possible that some disintegration of the subnitrite is produced in this manner. Undoubtedly the action only occurs after the bismuth has been some time in the intestine and exposed to the activity of the ferments, and long after the direct effect of the rays upon the bismuth has ceased. Lavage after the exposure or the employment of some other salt of bismuth will obviate the possibility of this accident.

Its value in determining the position of the colon is not yet, from a practical point of view, as great as its value in determining the position of the stomach for the reason that displacements of the colon are not nearly so amenable to medical treatment, if we can include in the methods of the internist the application of binders, rest in a horizontal position after eating, and other measures designed to facilitate the emptying of the stomach. On the other hand, as an indication for operative interference in those cases where the displacement of the colon is so great as to cause chronic constipation and various other disabilities it is of paramount importance and I believe can be replaced by no other method.

In consequence of our investigations upon enemata and the results of injections of bismuth into the colon I have reached the conclusion that it is not necessary to insert a rectal tube in giving injections into the colon further than the internal sphincter, that is for a distance of three or four inches. For over a year now I have followed this method, to the considerable comfort of my patients, without having had any reason to suppose that the enemata were not as efficient as by the usual method of the insertion of a

rectal tube for eight or nine inches. It has been my impression—unfortunately it is a subject upon which precise data are difficult to obtain—that the enemata were really much better retained than by the other method of injection.

Hospital for various lesions of the œsophagus and the gastro-intestinal tract has been increased to seventy-eight, and one hundred and sixteen radiographs have been made. Although, originally it had been the intention to describe the technique

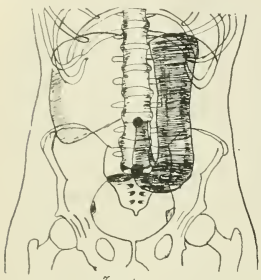
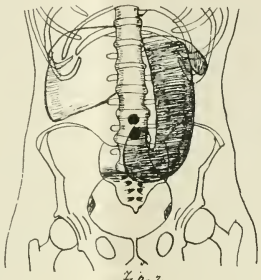


Fig. 1.



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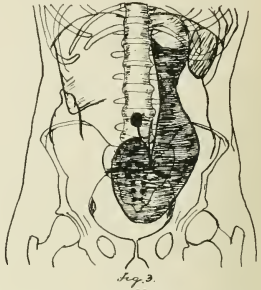


Fig. 3.

Fig. 1.—Gastroptosis, tubular shape, with dilatation, low position of the pylorus, and pyloric "kink."

Fig. 2.—The same patient, skiagraphed after application of an adhesive abdominal support. The umbilicus has been elevated with the flaccid abdominal wall. The effect upon the stomach seems to be a very slight elevation and alteration in contour of the greater curvature. The "kink" is less pronounced. There was more relief of symptoms than the skiagraphic appearance would seem to indicate. Referred by Drs. Sailer and Worden.

Fig. 3.—Extreme gastroptosis, with dilatation, low position of the pylorus, and a decided "kink." This is the typical shape of the stomach in the majority of cases of ptosis. The organ occupies a vertical position, and there is more or less narrowing below the cardiac end and the dilated fundus sags downward toward the pelvis. The skiagraph of this case shows the positions of the two flexures of the colon by the differentiation due to the collection of gas at these points. An operation was subsequently performed upon this patient. Referred by Dr. Sailer.

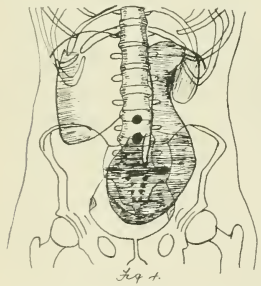


Fig. 4.

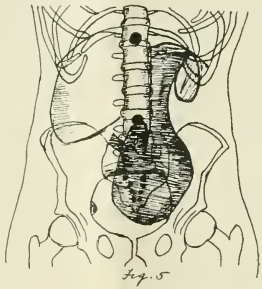


Fig. 5.

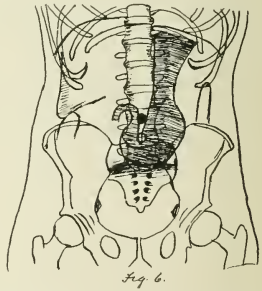


Fig. 6.

Fig. 4.—A case very similar to the preceding one.

Fig. 5.—The same patient, skiagraphed after application of an adhesive abdominal support. The umbilicus has been elevated with the abdominal parietes, but there is no change in the stomach except that the "kink" is not so sharp. Referred by Drs. Sailer and Worden.

Fig. 6.—A case with a lesser degree of ptosis and dilatation, but with a marked "kink." The pylorus occupies a position nearer normal. This patient was an unmarried young woman with exceptionally good physical development. Referred by Dr. Sailer.

THE TECHNIQUE AND VALUE OF THE BISMUTH METHOD OF X-RAY DIAGNOSIS IN THE GASTROINTESTINAL TRACT.

BY DR. HENRY K. PANCOAST.

Since the preparation of Dr. Worden's paper and up to the present time (June 15th) the number of cases examined by the bismuth method in the *x*-ray laboratory of the University

employed in the first forty cases examined in this manner, it seems proper that at this much later date we should include in this portion of the article a report of all cases referred to our laboratory up to the present time. Within a few months the field for *x*-ray diagnosis has been considerably broadened, as wider applications and greater possibilities have been found.

Most of our patients have been referred by members of the University Hospital and Dispensary Staffs. In addition to cases in their own private practices, Dr. Sailer and Dr. Worden have lent valuable experience and augmented the interest in the work by adding to the list patients from their services in other hospital dispensaries.

Our first observations were more of an experimental nature than for the application of any practical diagnostic value hard to realize that no practical use should have been made of such possibilities until November, 1905. It was at this time, however, that glowing reports from numerous sources awakened the medical profession to the fact that they had at hand a valuable and reliable method of diagnosis. It cannot be said that the very large experience of the past six months has given the least discouragement to our expectations.

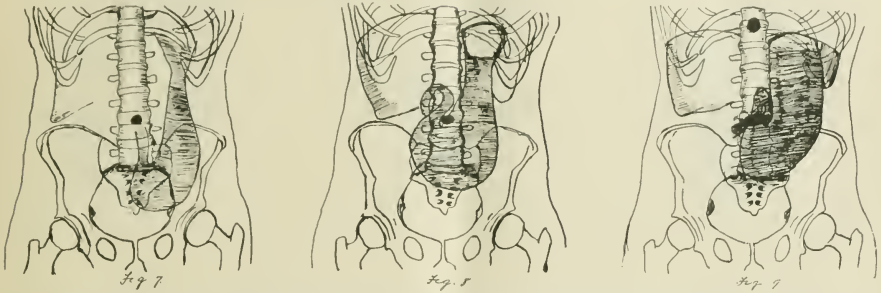


FIG. 7.—Gastroptosis, with "hour glass" constriction, with spasmodic contraction so tight that the bismuth suspension was introduced with difficulty. The patient subsequently underwent an operation. Referred by Drs. Sailer and Rhein.

FIG. 8.—Gastroptosis, marked gastrectasis, and pyloric "kink." Referred by Dr. Musser.

FIG. 9.—Gastroptosis and gastrectasis, without such marked elongation as is present in the preceding cases. Referred by Dr. Frazier.

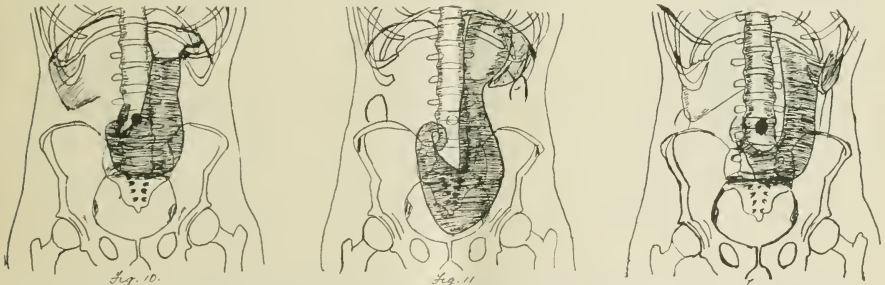


FIG. 10.—Moderate gastroptosis and gastrectasis, and low position of the pylorus, without a sharp "kink." Referred by Dr. Sailer.

FIG. 11.—Extreme gastroptosis and very much elongated stomach. Referred by Dr. Sailer.

FIG. 12.—Moderate gastroptosis with hypermotility and hyperacidity. The pylorus is low and there is no "kink." Referred by Dr. Sailer.

in the *x*-ray examinations. With a view of determining some facts in regard to reversed peristalsis in the large intestine several patients were skiagraphed after rectal injections of bismuth subnitrate in suspension. (See Plate V.) When it was found to be comparatively easy at that time to obtain satisfactory outlines of the colon, sigmoid, and rectum by what seems now to have been rather crude methods, it is

The *x*-ray examination by means of the bismuth shadow is applicable to every portion of the alimentary tract below the pharynx. The radiographic technique will be described as applied to the stomach, intestinal tract, and œsophagus in the order named. The examinations have been made entirely by the use of the skiagraphic plate. The loss of several lives, the necessary amputations of numerous fingers

and hands, and the existence of painful and practically incurable burns among *x*-ray operators, all due in a great measure to the use of the fluoroscope, should be a warning against any unnecessary use of this instrument for experimental purposes. These grave results, and unfortunately there are others equally serious, make it the most dangerous instrument in the hands of the physician, no matter how of time than any other *x*-ray work. The revelations of radiographs of the stomach have been surprising in a great many of the cases and the results of the examinations have invariably been of considerable value. Dr. Worden has called attention to the fact that in no two instances do the stomachs appear alike in shape, size, and position, and though this is certainly true, there are certain points of similarity that enable

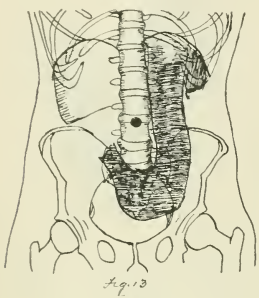


Fig. 13.

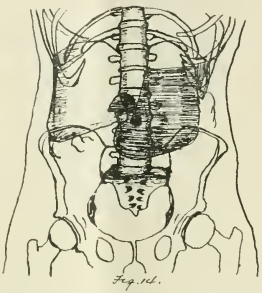


Fig. 14.

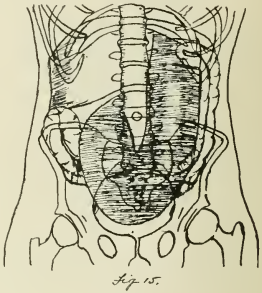


Fig. 15.

FIG. 13.—Marked gastroptosis, gastrectasis, low pylorus, without "kink." Referred by Dr. Sailer.
FIG. 14.—Moderate gastroptosis, gastrectasis, and tendency to kinking. Both flexures of the colon are low. Referred by Dr. Sailer.
FIG. 15.—Extreme gastroptosis and gastrectasis. Relatively high pylorus. Referred by Dr. Sailer.

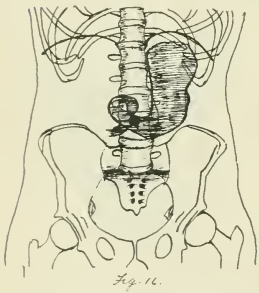


Fig. 16.

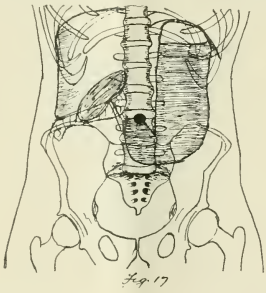


Fig. 17

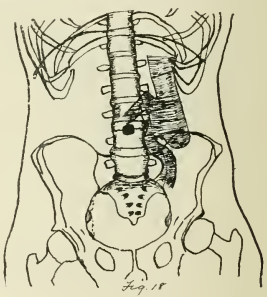


Fig. 18

FIG. 16.—Moderate gastroptosis, with hypermotility. Compare with Fig. 12. Referred by Dr. Sailer.
FIG. 17.—A composite diagram of two skiagraphs, showing a gastroptosis, movable right kidney, and liver displaced downward on deep inspiration. Referred by Dr. J. A. Scott.
FIG. 18.—Gastroptosis after gastroenterostomy. The bismuth is clearly seen escaping by both the normal and artificial openings. Referred by Dr. Sailer.

carefully it is used or what precautions are taken against exposure. Nothing much less than armor plate is impervious to the rays used in the examinations of this part of the body.

THE STOMACH. The examination of the stomach is the easiest of any portion of the tract, though it must be borne in mind that all of this work is tedious and is more consuming us to classify them roughly into several groups or types. In the accompanying cuts or diagrams we have endeavored to show at least one example of each class.

The details of the various steps in the radiographic technique follow:

1. Preparation of the patient. For a skiagraph of the stomach alone very little previous preparation is necessary

beyond having the stomach empty. In the absence of gastric retention a light and easily digested meal a few hours previous will not necessitate a preliminary lavage.

2. It is essential that no clothing shall be worn during the operation which will in any way interfere with the details of the skiagraph. Considerable exposure of the person is required in order to place the patient in proper relation to the plate and to bring the *x*-ray tube in relation to certain landmarks on the body. Unless this part of the work receives careful attention the result of the examination is valueless in determining the true anatomical relations. The exposure of the person is not a matter of much moment to male patients, but it is advisable with women to give due consideration to their feelings of modesty. We are in the habit of having our female patients retire to the dressing-room, where with the assistance of a nurse they don a muslin garment consisting of a cape and skirt. The cape, fastened around the neck with a draw-string, drops loosely to the hips and is easily lifted up back or front when adjusting the plate and tube. The skirt is held tightly around the hips and just above the pubes by a draw-string. There has never been the slightest objection to appearing in such a costume.

3. In order to produce a shadow of the stomach outline, some substance more or less opaque to the *x*-rays must be

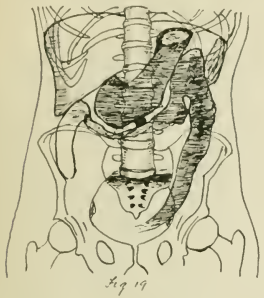


Fig. 19.

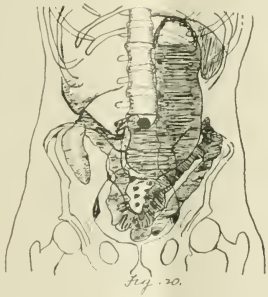


Fig. 20.

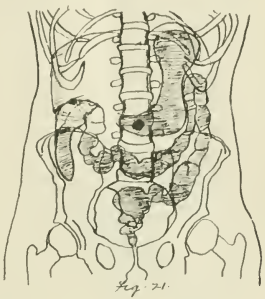


Fig. 21.

Fig. 19.—Stomach and colon nearly in what is supposed to be their normal positions. Bismuth introduced by mouth and rectum. Referred by Dr Musser.

Fig. 20.—Composite diagram of two skiagraphs, showing moderate gastroptosis and marked ptosis of the transverse colon and both flexures. Bismuth introduced by mouth and rectum. Referred by Dr. Sailer.

Fig. 21.—Composite diagram of two skiagraphs. Moderate gastroptosis and ptosis of transverse colon. Bismuth by mouth and rectum. Referred by Dr. Clark.

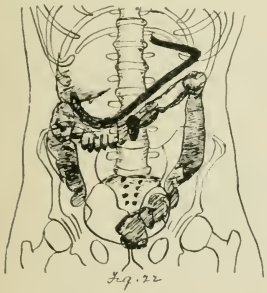


Fig. 22.

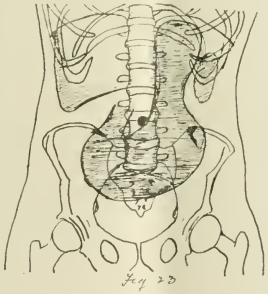


Fig. 23.

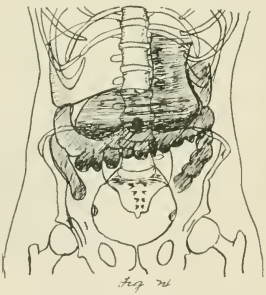


Fig. 24.

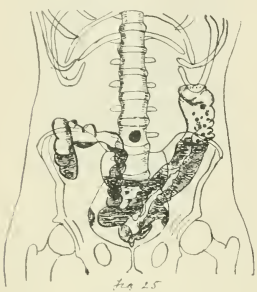
Fig. 22.—Gastroptosis, moderate, with gastrectasis. Very slight ptosis of the transverse colon. A stomach tube filled with powdered bismuth was introduced into the stomach. The uselessness of this method of outlining the stomach can be easily recognized. Colon injected by bismuth enema. Referred by Dr. Sailer.

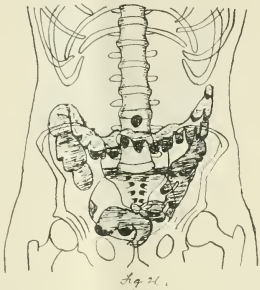
Fig. 23.—Gastroptosis and gastrectasis—before operation.

Fig. 24.—The same case, after operation. Bismuth by mouth and rectum. Referred by Drs. Tyson and Clark.

introduced. Invariably the subnitrate of bismuth has been employed, and may be given mixed with solid food, such as mashed potato, or suspended in milk or mucilage of acacia. The former method is perhaps preferable when the gastric motility is to be determined. It is a curious fact that so far none of our cases have been referred for this examination. Up to this time we have in all instances used a suspension of subnitrate of bismuth in mucilage of acacia in the proportion of two ounces of the powder to the pint. Even when carefully prepared the bismuth rapidly settles into a compact mass, and for this reason and because of the dangers attending the use of large doses of the subnitrate we are about to experiment with a special permanent chemical suspension of the subcarbonate in water. The objections to milk suspensions are the inability to keep them for any length of time and the difficulty of subsequent lavage on account of curdling. There are two methods of administration, either by the stomach tube or by having the patient drink the emulsion. We prefer the latter, first, because the patient does not have to take the tube twice if subsequent lavage is performed; and secondly, because, as Dr. Sailer believes, the bismuth begins to leave the stomach sooner. The pars pylorica and the duodenum are shown better, therefore, when the suspension is swallowed.

The amount of the mixture employed depends largely upon the results desired. In our earlier cases we used one quart of the suspension or four ounces of bismuth, as this quantity produced a dense and clear shadow, and represented





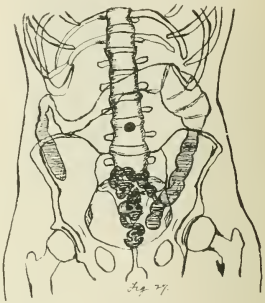
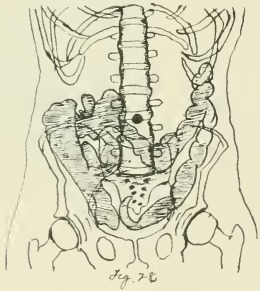


Fig. 25.—Ptosis of the transverse colon before operation.

Fig. 26.—The same case after operation. Bismuth by rectum. Referred by Dr. Clark.

Fig. 27.—Ptosis of the sigmoid. A composite diagram of two skiagraphs. The colon is in normal position, but is dilated above at the splenic flexure. The skiagraphic position of the sigmoid was subsequently confirmed by operation. Referred by Dr. Clark.



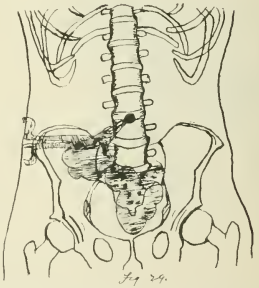


Fig. 28.—Carcinoma of the sigmoid. (Referred to in the text.) The bismuth shadow stops at the seat of constriction. Referred by Dr. Musser.

Fig. 29.—Obstruction in the jejunum. (Referred to in the text.) The rubber tube clamped by the hæmostat is in the fistula. Most of the bismuth has passed downward into the dilated loop of gut, although the attempt was made to force it above. The obstruction is at the apex of the triangular shaped shadow. Referred by Dr. Clark.

approximately the bulk and weight of an ordinary meal, including liquids. This amount, however, is not always sufficient to demonstrate the extreme degree of dilatation in all cases, but this difficulty may be easily overcome either by administering a larger quantity of a weaker emulsion or by having the patient drink the necessary quantity of milk before the emulsion is taken.

The dangers attending the administration of excessive doses of the subnitrate of bismuth are of sufficient importance to demand careful consideration. In addition to the four patients in whom toxic symptoms were observed, as reported by Dr. Worden, we have since had two more. In the first few cases four ounces of bismuth were allowed to remain in the stomach; there were no deleterious results, not even constipation; it was concluded that this drug was inert except for its sedative action, and non-toxic. But unfortunately there soon followed a series of cases in which there developed alarming but not dangerous toxic symptoms, very similar in each instance. In one to four hours after the administration the patients complained of nausea, or even vomited, especially when food was taken. They became markedly cyanotic, and were considerably prostrated. The pulse was rapid and full and the respiration rapid. These phenomena lasted several hours. For a time it was thought that they were manifestations, though not at all typical, of arsenic, or possibly antimony poisoning, despite the fact that the bismuth used was guaranteed to be free from such contamination. The absence of pain was ascribed to the sedative action of the bismuth. The last or sixth toxic case was a surprise, and was also peculiar in that the emulsion had been administered by enema only. Two ounces of bismuth were used and allowed to remain in the bowel. Absorption must have been confined entirely to the large intestine, because all of our experiments have so far shown that bismuth thus administered is not carried beyond the ileocæcal valve. It is possible that the toxic symptoms in this case may have been due entirely or in part to the fact that after the excessive purging attending the preparation of the patient, the walls of the bowel were unusually active in absorption under the sedative action of the drug.

Confronted by so many of these annoying accidents we determined to investigate the cause of the apparent poisoning. Two separate samples of the bismuth we were using were carefully analyzed by Dr. D. W. Fetterolf for the presence of poisonous impurities, and both were found to be absolutely free from any traces of either arsenic or antimony. It was then concluded that the toxic symptoms were the result of an idiosyncrasy on the part of some individuals to bismuth itself. About this time, however, a physician who was about to submit himself to a skiagraphic examination of his stomach suggested to Dr. Sailer that the symptoms as described to him were similar to the phenomena following the administration of excessive doses of the drugs of the nitrite group. This suggestion has been accepted as explaining the difficulty, and it has been concluded as probable that someone or more of the intestinal ferments under certain conditions and in some individuals are capable of decomposing the subnitrate of bismuth with the formation of a nitrite in amounts sufficient to cause toxic symptoms. This action may or may not be influenced by the *x*-ray. It seems improbable that this chemical change occurs in the stomach, as the phenomena are never fully manifest until some time after the administration, and bismuth in suspension, as we have employed it, does not remain in the stomach very long. Moreover, in one case it was confined to the large bowel only. Everyone knows that bismuth salts rapidly undergo chemical change in the intestinal tract. In cases of gastric hypermotility, in which the stomach contents pass rapidly and in bulk into the small intestine, these results might follow more readily. It is also possible that a subnormal peristaltic action of the small intestine may be a factor by allowing the drug to be acted upon more readily with the production of larger amounts of poisonous derivatives.

Whatever the cause of these accidents, it behooves us in the future to use every precaution to prevent dangerous results arising from the administration of large doses of bismuth. This method of diagnosis is of too great value and has been too widely adopted to allow us to give it up on account of such accidents. Our rule at present is not to leave over one-half ounce of the subnitrate of bismuth in the stomach unless the patient can be closely watched for several hours afterward, and even then not more than one ounce should be allowed to remain. If a larger amount has been administered the stomach is washed out as soon as possible after the skiagraphic exposure. One must be sure that the end of the tube reaches the most dependent portion of a ptosed stomach, as the heavy powder always settles there. When the colon has been examined after the bismuth enema a cleansing injection should follow, in order to remove a part, at least, of the retained drug, and a mild purge is also advisable. In gastric diagnosis the administration of bismuth in food will interfere with subsequent lavage, and we prefer not to use this method unless for the determination of motility.

There are a few other but less satisfactory ways of obtaining the picture of the stomach by the skiagraph. The original method of insufflation with dry powder is now obsolete, and the introduction of a stomach tube filled with powdered bismuth we have tried and found unsatisfactory and unreliable. (See Fig. 22.) Some radiographers prefer inflation of the stomach or colon. This gives a fairly reliable picture in thin subjects, but is not to be compared to the bismuth skiagraph, and this method is certainly no less uncomfortable to the patient and is not unattended with dangers.

4. The examination should be made while the patient

is standing, for in this posture the greater curvature and pylorus are sure to drop to their lowest level, especially with the stomach filled with the bismuth mixture. Moreover, it is in this position that patients with ptosis are more apt to have their symptoms aggravated, and is the one usually occupied during the day. Numerous instances have been cited in which the stomach occupied its apparently normal position, or nearly so, when skiagraphed with the patient lying on the back or side, but a second picture made while standing showed a marked gastroptosis. As the greater part of the stomach, except the cardiac end and the pylorus, approach nearer to the anterior abdominal wall than posterior, skiagraphs of this organ should be made with the plate in front of the patient and the tube behind, in order to give the best details and to reduce to a minimum errors of projection. If the patient is unable to stand, a picture may be made in the sitting posture.

5. In order to obtain a good and accurate skiagraph of this kind the proper kind of apparatus and its skilful manipulation are essential. Any radiographer of average skill can make satisfactory pictures of the stomach provided he uses a powerful coil and a suitable tube; but the most experienced operator will fail with inferior apparatus. No more beautiful examples of skiagraphic art can be obtained than those of the gastrointestinal tract, but they are without value unless what they portray is accurate. As in all other radiographic work, a stomach picture may be very misleading unless certain details of technique are carefully observed.

Short *x*-ray exposures are essential and in all persons of average build or thin people should not exceed fifteen seconds. There are several reasons for observing this rule. The patient must stand perfectly still of course. The breath must be held, for respiratory movements will prevent the obtaining of a clear outline. Lastly, the exposure must be sufficiently short to prevent peristaltic movements from interfering with the distinctness of the shadows. All of our skiagraphs have been made during full but not forced inspiration, simply because it is easier for the patient to hold the breath with the lungs well filled. Respiration has very little if any influence upon the position of the stomach, though it has been claimed that the greater curvature may descend considerably during forced inspiration. To confirm the findings of other investigators upon this point, two successive skiagraphs were made of one of our patients. The first, made during forced inspiration, showed the greater curvature little if any lower than the second taken during forced expiration. There was a slight change in the shape of the organ.

6. A few universally accepted landmarks are necessary for the proper interpretation of these radiographs. The vertebræ, iliac crests, anterior superior spines, and the pubic crests are the normal anatomical bony points, but the position of the umbilicus must always be marked. The shadow of this landmark may be made on the plate by placing a small coin over the spot. If this is to be the point from which measurements are to be made the skiagrapher must be certain that the anticathode of the tube is in the same horizontal plane as the umbilicus and as nearly as possible in the same vertical plane with it and the spine. It is often desirable to mark the level of the tip of the ensiform, and this may be done in the same way as the umbilicus.

The Colon and Sigmoid. The entire large intestine may be skiagraphed by the bismuth method, but with a few exceptions to be mentioned later satisfactory pictures of the small bowel, except possibly the duodenum, have not yet been made. The patient requires more preliminary preparation than in stomach work, as the intestinal tract must be emptied previously by thorough, but not excessive, purgation, and just before administering the bismuth suspension by rectum a simple cleansing enema should be given.

The usual method employed is to administer the mixture through a soft rectal tube of as large a lumen as possible. The tube should not be introduced farther than three or four inches, or just beyond the internal sphincter. The best results are obtained by observing this rule. The enema must be given slowly, and no force used either by the syringe bulb or gravity beyond about one foot pressure. The principles applied here are different from those of giving high enemata for other purposes. We wish to guard as much as possible against the bismuth being carried toward the cæcum by any force except that of antiperistalsis. The one great secret of the operation itself is to allow the liquid to simply trickle through the tube. Once the outlet of the funnel and the lumen of the tube become completely filled it is almost impossible to get the mixture to run in satisfactorily. The amount usually introduced is one pint of the suspension, representing two ounces of the bismuth salt. When the tube is removed the patient should remain in the recumbent posture for thirty to forty-five minutes before the *x*-ray exposure is made. This time is adopted as a result of the investigations of Dr. Sailer and Dr. Worden in our laboratory about three years ago. This was the average period required for the bismuth mixture to be carried by antiperistalsis as far as the cæcum in sufficient quantity to ensure a satisfactory skiagraph. When radiographing the colon the length of exposure, position of the plate and tube, posture, and landmarks are the same as in the technique for the stomach.

It is often of advantage to have the bismuth reach the colon by way of the stomach and small intestine, especially when determining gastric and intestinal motility, or searching for the seat of a partial obstruction in the bowel. Ordinarily, the bismuth given in suspension should reach the colon in amount sufficient for a skiagraph in twelve to eighteen hours.

The lower portion of the sigmoid and the rectum are shown best by placing the plate behind the pelvis of the patient, who may be either in the erect or recumbent posture.

Whenever it is necessary or possible to radiograph the ileum or jejunum the bismuth must be introduced by way of the stomach, in the absence of a fecal fistula, and the plate is exposed in the same manner as for the colon.

Œsophagus. Aside from the detection of the presence of lodged foreign bodies, the œsophagus offers the greatest difficulty of any portion of the alimentary tract to *x*-ray diagnosis, not only for anatomical reasons, but because of the rapid movements of deglutition preventing the lodgment of any opaque substance, such as bismuth. The application of skiagraphic diagnosis is limited practically to the determination of the presence, extent, and site of constrictions, and diverticula. Unfortunately, the number of cases referred to our laboratory during the last six months has been very small and we have been unable to give to any particular modification of the bismuth method a satisfactory trial. Two cases have been skiagraphed with accurate diagnostic results, though the artistic appearance of the plates was poor. In one a partial stenosis high up was found, and in the other a possible malignant stricture low down was excluded. In both cases the radiographic findings were confirmed at autopsy. It must be admitted that our method of having the patient swallow dry powdered bismuth and washing it down with a small quantity of emulsion is crude, and in the future another way of filling the œsophagus will be tried.

The Value of X-ray Diagnosis.

Diagnosis by means of the *x*-ray has been found of greatest value probably in such conditions as fractures and dislocations, foreign bodies, joint disease, and renal calculus; but it seems like a conservative statement to say that we may expect the application of the bismuth method in determining certain conditions of the gastrointestinal tract will in the near future be the next in the order of usefulness. Were it not for the value of this kind of work and the interesting results obtained the tediousness of the dark-room development would give the radiographer sufficient reason for not advocating its frequent application. If the operator is careful in every detail of his technique the results are certain to be accurate. This cannot be said of other methods of examination. The plate shows exactly what is to be shown, and a skiagraphic error is the fault of the radiographic technique or the interpretation of the skiagraph.

There are certain gastric conditions which may be determined with precision, such as the presence and degree of gastroptosis, gastrectasis, the position and shape of the stomach, the situation of the pylorus and lesser curvature, which is often difficult by other means, the existence of a kink in the pars pylorica, and frequently the results of operation and other forms of treatment. Motility of the stomach may be studied by repeating the first skiagraph made after introducing the bismuth in about six hours, and subsequently as often as desired. A reasonably certain diagnosis of early carcinoma would be of great value, but as yet this is a very remote possibility. In one of the three cases of this kind examined, the appearance of the stomach was sufficiently characteristic to warrant a positive opinion, but the disease had reached such an advanced stage that the diagnosis was almost certain clinically, and was confirmed by an exploratory operation later.

The intestinal tract offers a wide field to the search for practical applications of this method of diagnosis. Little can be accomplished in the jejunum and ileum, but in the one patient examined the results were of considerable value. The case was one of partial obstruction in the jejunum, with a fecal fistula near the point of constriction. A previous operation for the relief of obstruction by adhesions could not be completed on account of the alarming condition of the patient, and an enterostomy was necessary as a palliative measure. Dr. Clark referred the case, with the object of determining the seat of obstruction and its relation to the fistula, and whether a constriction existed both above and below the opening. This knowledge was desirable before performing a second operation. Dr. Clark prepared the patient for the skiagraphic examination by injecting into the fistulous opening several ounces of bismuth emulsion. A few ounces of the mixture were swallowed in order to outline the stomach and duodenum. The skiagraphs demonstrated clearly the absence of constriction below and the presence of the obstruction a short distance above the fistula. This condition of affairs was confirmed a few days later and the operation was considerably shortened by the information gained by the examination. (See Fig. 29.)

Two cases of fistula communicating with the descending colon have been examined and their connection with the bowel shown. In one instance the bismuth outlining the colon was administered by mouth because of the inability to introduce it by rectum, and in the other an enema of the suspension was given. In each case a small quantity was injected into the fistulous tract.

Valuable information has been obtained from skiagraphs of the colon. The method of introduction of the bismuth, whether by way of the stomach or by enema, must be selected as best suited to each individual case. Ptosis of the transverse colon and one or both flexures has been easily diagnosed in several patients, and in a few in which adhesions were suspected because of the close relation between two loops (Plate IV.), this condition was confirmed by subsequent operation. The seat of malignant stricture in the descending colon was shown after rectal injection of bismuth in one

case, and in another in which cancer of the colon was suspected the skiagraph revealed a very marked ptosis of the transverse colon without any constriction at any point. Thorough purgation proved the obstruction to be fecal.

One case of malignant stricture of the sigmoid has been examined and the seat of the disease located. The bismuth was introduced by way of the stomach because the obstruction was low down. (See Fig. 28.) Several examinations have been made for ptosis of the sigmoid, with a positive result in two cases, and in one of these (Plate VI.) the diagnosis has been confirmed by operation. (See Fig. 27.)

One of the patients skiagraphed for malignant obstruction of the large bowel subsequently passed a large mass of bismuth that had evidently settled in one of the pouches of the rectum or sigmoid. This incident suggested a possible danger of acute obstruction resulting in such cases if such a mass dislodged from one of the pouches above the seat of disease should become impacted within the area of constriction.

A résumé of the cases examined follows:

Gastroptosis, examined, 50; positive diagnosis, 49 (males 20, females 29).

Gastroptosis and ptosis of colon, 6; positive diagnosis, 5.

Ptosis of colon, 8; positive diagnosis, 7.

Ptosis of sigmoid, 4; positive diagnosis, 2.

Carcinoma of stomach, 3; positive diagnosis, 1; unsatisfactory, 2.

Œsophageal stricture, 2; positive diagnosis, 1; negative, 1.

Intestinal obstruction, 4; positive diagnosis in all; carcinoma of colon, 1; carcinoma of sigmoid, 2; obstruction by adhesions, 1.

Fecal fistula, 3; satisfactory results in all.

Cases used for experiments on antiperistalsis, 3.

The accompanying diagrams were made from the skiagraphic negatives and every effort was made to preserve the anatomical relations as shown on the plates.

REMARKS BY DR. G. G. DAVIS.

Considering the normal relations of the stomach we find its cardiac end situated beneath the seventh costal cartilage one inch to the left of the sternum, about opposite the upper part of the eleventh thoracic vertebra. It is attached to the diaphragm and suspended to the œsophagus. The peritoneum does not embrace it closely, but, particularly on its posterior or under surface, is some distance away. For these reasons the cardiac extremity is practically fixed and retains its position even when the stomach is distended, dilated, or prolapsed. The pylorus is in the midline and moves as much as two inches toward the right when the stomach is distended. It lies opposite the first lumbar vertebra approximately midway between the tip of the xiphoid cartilage and the umbilicus. The greater curvature rises higher in the left hypochondrium than the level of the cardiac opening and descends in the median line to a lower level than the pylorus, its lower edge being two to two and one-half inches above the umbilicus, and may, even when normal, be level with it, thus bringing it opposite the body of the third lumbar vertebra.

The pylorus is almost entirely surrounded by peritoneum, as is also the duodenum, for its first inch.

Thus we see that the pylorus is extremely movable within a short radius. The next eight or nine inches of the duodenum are, however, firmly fastened to the spine and the structures lying on it being covered by the peritoneum only in front. Thus it is seen that extensive displacements of the pylorus are combated by the firm duodenal attachments.

The lesser or gastrohepatic omentum acts as a suspensory ligament for the stomach, but it is attached to the lesser curvature and stretches as it descends.

These anatomical facts should be borne in mind in studying both the physiology and pathology of the organ. It has recently been impressed on the medical mind that the position of the stomach is more vertical than has usually been considered to be the case. But when we remember that the cardiac end is opposite the eleventh thoracic vertebra and the pylorus opposite the first lumbar we see one is only two and one-half to three inches lower than the other, so that if the stomach is normal it must of necessity be more horizontal than vertical. The question arises, what is its position when dilated? It is obvious that the cardiac end remains in place, but the stretching of the gastrohepatic omentum allows the greater and lesser curvatures to descend. To what extent the pylorus descends is still to some extent in doubt.

From the firmness and extent of the attachments of the duodenum one would expect it to be held up, but recent skiagraphs have suggested that it too descends. Caution should be observed in interpreting these skiagraphs. It seems almost impossible that the pylorus should ever be found in the pelvis. We are in need of accurate postmortem examinations to determine the position of the pylorus and duodenum in cases of marked ptosis.

The shape of the stomach and even the duodenum is variable. While it is sometimes found postmortem to be of the usual pear-shape, it is not rare to find in formalin hardened bodies that for one-third of its distance from the pylorus the stomach is contracted to the size of the duodenum. This is the motor part and the remaining two-thirds is the resorvoir and in dilatation it is mainly this portion which is dilated and which prolapses down even into the pelvis. The hour-glass condition is probably normal in certain periods of digestion, as it is often found after death where no organic lesions are present. At times the pyloric end also may be dilated, and even the duodenum itself may be found

B. J. C

markedly dilated though not markedly depressed. The shape and position of the stomach is also of interest in relation to its percussion. Ordinarily, there is only an inch or two visible in the median line beneath the edge of the liver with the transverse colon just below it. It is obvious that if, as is often the case, the pyloric third of the stomach is contracted to the size of the duodenum it will give almost or quite a flat tone. I have even seen a couple of coils of small intestine lying next to the edge of the liver with a small part of the stomach visible lower down and the transverse colon below it.

All of which tends to make clinical observations on the stomach, as the region of the median line is approached extremely unreliable.

PECULIAR PRESSURE SYMPTOMS DUE TO ENLARGED TUBERCULOUS BRONCHIAL GLANDS.

By Thompson S. Westcott, M.D.,
Philadelphia.

The following case is considered worthy of record chiefly on account of the unusual pressure symptoms observed during life; but is not less interesting because of the occurrence of tuberculous disease in very early infancy and the recognition of the probable source of the infection dating back to the earliest days of life.

The baby, a girl, was born about the middle of February in one of our city hospitals, the mother having taken a private room for the purpose because of the inconvenience attending confinement at home in a boarding house.

The labor was uneventful and the baby was satisfactorily nursed by the mother from the time of birth until its death at the age of four months, and had never received artificial feeding.

The father and mother of the child are apparently in good health. The first child of the family, then about two years of age, was seen by the writer, in consultation, about six or seven years ago, a few hours before death from enterocolitis. This child was rachitic and had a minor degree of hydrocephalus, but was not known to be tuberculous, although the question was raised at the time on account of a family tendency on the mother's side. No autopsy was made. A second child, then about four years old, was seen by the writer in 1901 and treated for a chronic diarrhœa, which the father feared was tuberculous. She recovered, however, and is to-day an apparently healthy and well-nourished child.

The subject of this report first came under the writer's notice on April 29th, when she was just past three months of age. She was fairly well-nourished and well-developed for her age, the upper part of the chest being noticeably high and full. She had thriven well on the breast milk, which she took with normal appetite, until about the age of two months, when the appetite began to fail and she did not nurse so well as she had previously; but until a few days before the first consultation nothing was thought to be amiss.

The stools then became too frequent and showed signs of indigestion, and for this reason I was first consulted. On inspection it was noticed that the baby breathed with effort and seemed as if the deep and somewhat slow respirations tired her. Examination of the lungs showed a weakened respiratory murmur over the upper part of the left lung, but no rales and no evidence of consolidation. The temperature was about normal and the pulse good. The cheeks showed some stellate capillary venous enlargements, and the larger veins about the eyes and on the temples were noticeably full and clearly marked. Venous enlargements were noted over the anterior surface of the chest.

She was seen again on May 2d. The digestive trouble was better but the condition of the lungs was still the same. It was noted now for the first time that the child seemed to be uncomfortable when held up in the mother's arms and the fingers and hands seemed to be slightly congested, this appearance passing away when the baby was put flat on the back, in which position the mother said it seemed to rest most comfortably. In the following week the child developed chicken-pox, contracted from her sister. The lesions were not numerous and she was not much affected. I was not called to see her until May 8th, when the vesicles were drying up. At this time the evidences of intrathoracic pressure had become more distinct, so that when held in a somewhat flexed position in the mother's arms the whole head, neck, and arms became distinctly cyanosed, the discoloration fading when the child was laid flat on the bed. A slight degree of fever was now manifest, reaching 101° on the 9th, and ranging from this down to normal on the 10th and 11th. On Thursday, May 12th, the temperature became somewhat higher and nourishment by the breast was taken fitfully and in insufficient amount, the usual position seeming to cause the baby discomfort and produce the cyanosis of the head and upper extremities, so that the mother adopted the expedient of bending over the child lying flat upon the bed, and in this position better

results were obtained. The upper part of the right lung now began to show signs of bronchopneumonia, the temperature became higher and remained about from 101° to 102° until May 20th, when it began to fall gradually. The respiration continued heavy and labored. Nourishment was given by pumping the breast and giving the milk by spoon and a concentrated food was given in addition. The child was seen for the last time during life on May 20th. Cyanosis of the fingers and hands up to the wrists was variable but constantly present in some degree, and in certain positions in which the vertebral column was curved forward, the arms, neck, shoulders and head became cyanotic, but the discoloration would largely subside when the position was changed so as to straighten out the vertebral curvature. The pulmonary signs in the right lung remained about the same. The bowel movements had been somewhat frequent during the whole of this week, the stools at times good, and again consisting of brownish mucus, alone, or mixed with normal feces.

Death occurred quietly on May 21st, a few hours before my visit.

The diagnosis was a probable pulmonary tuberculosis with some pressure upon the descending vena cava probably dependent upon tuberculous enlargement of bronchial glands.

At the autopsy, which was made with the assistance of Dr. C. H. Weber, both lungs were found thickly studded with miliary tubercles, the right one in its upper lobe showing the appearances of a recent bronchopneumonia. At the root of the lungs and in such a position as to press upon the trachea to some degree, but more particularly upon the descending cava, was a mass of tuberculous glands the size of a pigeon's egg, the centre of one of which had broken down and contained about twenty minims of purulent fluid. A few scattered tubercles were found in the spleen. The liver and other abdominal organs were free from gross evidences of the disease. The heart was normal and not involved.

The mechanism of the cyanosis was readily understood. The tuberculous glands had pressed upon the descending cava, and in the positions in which the upper part of the chest was bent forward sufficient pressure had been brought to bear upon the cava to materially interfere with the free return of blood to the heart from the head and upper extremities. When the child was in the supine position there had been little interference with free circulation. It is quite likely that a certain amount of pressure had been exerted upon the trachea or the main bronchi, but this is hardly sufficient to explain the air-hunger which the baby manifested for three or four weeks before its death. This seems to have been due in large part to the interference with free aeration produced by the encroachment of the very numerous miliary tubercles scattered throughout both lungs. The weak breath sounds early noticed over the left lung were more likely due to the tuberculous involvement of the parenchyma of that lung, as the principal mass causing pressure over the vena cava was rather toward the right than the left side.

In discussing the possible origin of the infection with the parents the mother stated that at the time of her confinement at the hospital a patient was dying of pulmonary tuberculosis in another private room across the hall from her room, and questioned whether this case might not have been the source of the infection of her baby. The facts that signs of the disease as shown by failing health were noticed when the child was only two months old, and that the large bronchial gland showed advanced disease, make it certain that the original infection must have occurred soon after birth. The absence of appreciable involvement of the intestinal canal and the fact that cows' milk as a possible source could be absolutely excluded, point to inspiration as the method of infection, and the bronchial gland as the original focus.

As far as can be learned the child was kept under good hygienic conditions after leaving the hospital, and its tender age and the season of the year (middle of February to middle of April) make it unlikely that exposure occurred outside of the house. As far as the parents could tell the baby had come in contact with no one suffering from tuberculosis or had been exposed to the surroundings of tuberculous patients at any time, other than in the hospital. While of course such speculation is productive of little definite results, I cannot but feel that the presence of a case of active tuberculous disease within a few feet of the room in which this baby was born, offered a quite possible source of infection, either through the medium of dust or more directly perhaps through the intermediary of nurses who in all likelihood attended to the needs of both the tuberculous and the maternity patient and her baby. Infected fingers of a nurse or resident physician might well have carried the disease directly to the baby if either of them had the reprehensible habit of senselessly sticking a finger into a baby's mouth.

BOOK REVIEWS.

A Reference Handbook of the Diseases of Children. For Students and Practitioners. By Professor Ferdinand Fruhwald, of Vienna. Edited, with additions, by Thompson S. Westcott, M.D., Associate Professor of Diseases of Children in the University of Pennsylvania. Octavo, 553 pages, with 176 illustrations. Philadelphia and London: W. B. Saunders & Co., 1906.

This good book, so popular abroad, has been well, perhaps too faithfully, translated. Each subject is treated in a brief article which will prove interesting and instructive to anyone who uses such a book of reference; yet the space devoted to drugs in the treatment of the various conditions seems appalling from the American point of view. Even Dr. Westcott feels constrained to object to several of the large doses mentioned in the text, and also to the use of opium in appendicitis. He has amended the German plans of infant feeding, which differ so radically from our notions. An eminently foreign idea in this book is the stress laid upon the therapeutic value of the various drinking and bathing resorts, something always prominently mentioned in European textbooks.

The articles on chorea, cretinism, diphtheria, lymphadenitis, measles, rachitis, spondylitis, syphilis, and tuberculous meningitis are excellent. The alphabetical arrangement of the subject matter may be of value to a student in a hurry, but it separates subjects which belong together, as, for example, bronchitis, capillary and catarrhal; pneumonia, cholera infantum, and the gastrointestinal diseases of infants. Several points of less importance are mentioned which are rarely found in any text-book, but laryngismus stridulus is omitted. The long article on scrofulosis will interest young American physicians. The illustrations are very good, among the best being the one showing achondroplasia. For procuring these, many of which are the original German illustrations, and for his accurate, painstaking, and faithful translation, Dr. Westcott deserves great credit. M. O.

Diseases of the Eye. A Handbook of Ophthalmic Practice. By G. E. de Schweinitz, M.D., Professor of Ophthalmology in the University of Pennsylvania. Fifth edition, revised and enlarged. Octavo, 894 pages, 313 text-cuts and six chromo-lithographic plates. Philadelphia and London: W. B. Saunders & Co., 1906.

Upon reading through the contents of this book we are impressed by the remarkable fulness with which it reflects the notable contributions recently made to ophthalmic literature. The new edition has been enlarged by about one hundred pages, and no important subject within its province has been neglected.

Of the portions which have been rewritten, several chapters deserve praise and recommendation. The chapter on the "Pupil and its Anomalies" is in itself a complete treatise. The "Varieties of Conjunctivitis" are concisely described and placed in nearer etiological relations to each other than formerly. The perplexing and complex subject of the "Pathogenesis of Glaucoma" is lucidly set forth, and the "Pathogenesis and Pathology of Sympathetic Ophthalmitis" are as clearly defined as modern research will allow.

The chapters on the treatment of wounds of the globe, especially when the wounds have been caused by a penetrating and afterward retained foreign body are most explicit and practical. The great advances that have been made in the surgery of the eye since the use of radiography for the localization of a retained foreign body, as well as in the use of specially designed electromagnets for the extraction of the foreign body, are carefully detailed.

The author has not failed to present for consideration the newer chemical and organic compounds recently introduced into ocular therapeutics, and he frankly gives his own experience in the use of them.

Of particular interest are the chapters touching upon those subjects which might be included under the head of "Medical Ophthalmoscopy."

Indeed, after reviewing Professor de Schweinitz's book, one is compelled to acknowledge it to be the most complete treatise in the language. And as we read its pages there is forced upon us the conviction of how large a part Ophthalmology has in the science of Medicine. It embodies in itself the principles of the early Greek physicians, to whom "external" and "internal" medicine did not exist, and the time ought not to be far distant when this division of the science shall be removed and we shall see with the clear eye of the Greek, to whom medicine and surgery were one.

This book presents substantially the same appearance as in the former editions, yet it has attained to even a higher standard of book-making. The illustrations have been revised carefully and over thirty have been added, while the index of fifty pages makes one wish that such things might be "made in Germany." B. K. C.

The Operating Room and the Patient. By Russell S. Fowler, M.D., Surgeon to the German Hospital, Brooklyn, New York. Octavo, 172 pages. Philadelphia and London: W. B. Saunders & Co., 1906.

In Dr. Russell Fowler's book we have a work which is well adapted to the use of nurses who are about to take charge of an operating room, or doctors who are to become internes in hospitals, or those who desire to take up surgical work without previous hospital experience. It is full of very useful information which it is difficult to find elsewhere. It describes the preparation of various materials, indicates the instruments for different operations, gives an illustrated description of the various positions of the patient for each operation, and details the preparation and after-treatment of surgical cases.

There is a chapter on anæsthetics describing indications for the various anæsthetics and modes of administration.

This book is written for those untrained in surgery and the operating room, and is, as Dr. Fowler says, only a forerunner to a larger and more thorough work on postoperative treatment. M. B.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

CEREBRAL DECOMPRESSION.

Palliative Operations in the Treatment of Tumors of the Brain, Based on the Observation of Fourteen Cases.[1]

By William G. Spiller, M.D.,
Professor of Neuropathology and Associate Professor of Neurology in the University of Pennsylvania,
and
Charles H. Frazier, M.D.,
Professor of Clinical Surgery in the University of Pennsylvania.

remarks by dr. spiller.

Palliative operations in cases of brain tumor are not new, and the temporary benefits to be derived in this way have been fully recognized by many physicians during many years. It has seemed time well spent to examine some of the reports of cases treated by trephining, or other method of opening the skull, for the relief of pressure when a tumor could not be localized, or if localized could not be removed. Unquestionably many cases have been omitted, and yet I have collected sufficient to demonstrate that palliative treatment has an important place in cerebral surgery.

review of literature.

Annandale[2] said, in 1894, that more than twenty years previously he had opened the skull of a patient whose symptoms were those of general brain pressure and, although no special condition was found, temporary relief was marked. Another case of this kind, he says, was operated on by Sir Joseph Lister in the same wards with success. In 1889, Annandale removed a piece of bone from the skull because of intense headache, following an injury of the head years previously. No abnormal condition was found, although the dura was incised. The patient made an excellent recovery and was perfectly cured. Annandale remarked that when no localized symptoms of brain tumor exist an exploratory operation may be performed, and experience has shown that in some of these cases the operation has been useful in taking off general pressure and in a few instances has even been followed by shrinking or degeneration of the growth. Again, a growth may give rise to effusion of fluid or to hemorrhage, and the symptoms caused by these conditions may be at least temporarily removed by the operation.

Sahli,[3] in 1891, spoke of improvement from palliative operations. The tumor in one case was supposed to be in the cerebellum. Vision improved and headache disappeared after a palliative operation. The patient (a boy) died some months later and no necropsy was obtained. Sahli thinks that two trephinings remote from each other give more relief of pressure than one. Sometimes Nature performs a palliative operation, what he calls *Selbsttrepanation*. In consequence of the pressure the skull becomes thin at the region of the Pacchionian bodies and openings may occur, and in one case he saw the brain protruding through several such openings.

The palliative operation, he thinks, is not ideal, is not without danger, and improvement is only temporary. In one case of prolapse of the brain he observed unconsciousness immediately followed by death. Acute prolapse of the brain may impair the function of the rest of the brain. He recommends small trephinings in preference to large.

In 1891, White[2] described a number of cases of epilepsy in which improvement followed operation, although nothing abnormal was found.

In 1893, Horsley[3] said that the removal of excitatory symptoms by opening the skull is a marked phenomenon, convulsions ceasing. In one of his cases in which the diagnosis of tumor of the middle cerebellar peduncle was made the skull was opened only to relieve the pressure, and the cerebellum protruded almost an inch through the trephine hole. The symptoms of tumor soon disappeared, and six months later the man felt perfectly well. He survived eighteen months, and during this time had few attacks. Instead of a tumor only a small cavity was found.

[1] Read in the Section on Nervous and Mental Diseases of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906, and published simultaneously in the Journal of the Association.

[2] Edin. Med. Jour., January to June, 1894, p. 898.

[1] Volkmann's "Sammlung klin. Vorträge, Innere Medicin," Nos. 1 to 29, 1890–1894, p. 300.

[2] Annals of Surgery, August and September, 1891.

[3] Brit. Med. Jour., 1893, No. 2, p. 1365.

Horsley thinks that some tumors are so interfered with in their nutrition by opening the skull and suddenly altering the pressure therein that they forthwith degenerate. In another of his cases the tumor was too large for removal, but the patient survived for over two years, with disappearance of the attacks and improvement of the hemiplegia. The tumor at the time of the operation was obviously malignant and rapidly growing, but had later undergone complete destruction by the mere exposure at the time of operation. Such a result, he says, cannot be anticipated or expected as likely to follow, but it is an argument in favor of opening the skull for the purpose of palliating a condition which cannot be cured.

Horsley says, also, that he has found in every case the effect of opening the skull has been to remove the headache, and, further, that in cases where it was known before operation that the tumor could not be removed, relief from severe pain afforded by opening the skull persisted until the patient died. The simple and safe procedure of opening the skull should be undertaken when drugs fail. At the Berlin Congress Horsley pointed out that opening the skull caused the swelling of the optic disks to subside, and that the subsidence may proceed steadily to complete recovery, provided atrophy has not previously begun. If atrophy has commenced the condition is hopeless. Vomiting is dependent on the degree to which intracranial tension is raised, and, as a rule, this symptom disappears when the skull is opened.

Jaboulay,[1] in 1893, obtained good results by trephining in a case of tubercle of the brain without opening the dura. The prognosis from trephining, he thinks, is better the more superficial and circumscribed the lesion is.

Caton and Paul[2] trephined the skull in a case of acromegaly in 1893. The dura bulged in the opening. The operation relieved the headache, and the remaining three months of the patient's life were comparatively comfortable.

Macewen[3] did a palliative operation in 1889 in a case with symptoms of cerebellar tumor. The patient experienced great relief. After a week tuberculous tumors were removed from the cerebellum.

Taylor[4] reported a series of cases of brain tumor to show that there is almost invariably a subsidence of optic neuritis after operation whether the tumor is removed or not. This fact, he says, was known to Horsley so long ago as 1888. In discussing Taylor's paper Horsley said that if there is any atrophy present no amount of reduction of pressure within the skull will produce the slightest change or afford the slightest relief in respect of the loss of vision. If there be commencing atrophy after operation the neuritis that may be present will disappear, but the atrophy is permanent; opening the skull, therefore, is not justifiable if the atrophy is well marked. Horsley was probably referring to the operation only in so far as vision is concerned, as the operation may relieve some of the other symptoms, even though it may be too late to restore vision. The optic neuritis may disappear, Horsley says, even though the dura is not opened.

In a case reported by Keen,[1] in 1894, the diagnosis of intracranial tumor was made, but the growth could not be located. Trephining was recommended with a view of relieving intense headache. The tumor could not be found.

The bone was not replaced, and, although the brain bulged greatly, headache and hallucinations entirely disappeared, and the man became a quiet and tractable patient. He died four and a half months after the operation, having been much relieved during this time. The operation was performed in 1892. In another case, also, much benefit was obtained by a palliative operation.

Bruns,[2] in a case of brain tumor in which the tumor could not be found at operation, improved the patient's condition by opening the skull. By the end of the third week very little choked disk remained, attacks of blindness no longer occurred, headache was much less severe and vomiting ceased. Similar improvement he had noticed in two other cases of brain tumor after trephining.

Byrom Bramwell,[3] in 1894, said that he had advocated trephining for the relief of symptoms in his book, *Tumors of the Brain*, published eight years previously, but that he would advocate the operation still more strongly in 1894 in cases in which there is a great increase of intracranial pressure and drugs have failed. When he published his book he had not been aware that Grainger Stewart or anyone else had recommended the operation. In many cases the headache is intense, and it has been shown that in some of these cases sudden death occurred, apparently as a result of the mere severity of the pain and sudden inhibition of the action of the heart. In other cases in which the intracranial pressure is greatly increased, the patient dies suddenly in an epileptic fit or as the result of failure of respiration. Opening the dura reduces intracranial pressure and relieves headache and other symptoms, among them optic neuritis.

In 1891, Kammerer[4] reported a case of supposed tumor of the brain in which double trephining was done for the relief of pressure. The headache disappeared, vomiting ceased for several weeks and then occurred occasionally.

[1] Arch. provinc. de Chir., 1893, vol. ii.
[2] Brit. Med. Jour., Dec. 30, 1893, p. 1421.
[3] Ibid., Dec. 23, 1893, p. 1367.
[4] Transactions of the Ophthalmological Society of the United Kingdom, 1893–1894, vol. xiv, p. 105.

[1] Amer. Jour. of the Med. Sciences, January and February, 1891.
[2] Neurolog. Centbl., 1894, p. 20; also 1893, p. 389.
[3] Edin. Med. Jour., January to June, 1894, p. 1067
[4] Annals of Surgery, January to June, 1894, vol. xix, p. 685.

The motive power of the right side (previously this side was paretic) improved and some sensation returned. The dura was not incised.

Wyeth remarked that he had trephined in two cases with symptoms of brain tumor, and, finding no tumor, had sewed up the dura, but had not replaced the bone; improvement had followed the relief of pressure.

Sänger,[1] in 1894, reported a case of brain tumor in which after opening the skull and dura prolapse of the brain with improvement in the symptoms occurred.

In one of the cases of tumor reported by E. Albert,[2] in 1895, in which palliative trephining was done, headache disappeared, but vomiting persisted. The dura probably was not opened. Later trephining was done on the other side of the head, but vomiting persisted. The relief afforded in this case was in regard to headache and might have been greater if the dura had been opened.

In another case in which trephining was done for brain tumor the dura was punctured. Headache became at once less severe, but the improvement was only temporary. In another case after trephining apparently without opening the dura, vision improved and headache and vertigo disappeared. The symptoms returned and the dura was opened. The operation was not very successful as a palliative means.

Schlesinger,[3] in a case of brain tumor, had a large protrusion of the brain as a result of the operation. The protruded portion could not be replaced, nor was it excised, and when the patient was presented he had a subcutaneous tumor on his head as large as a fist. The general condition improved as a result of the operation, the palsy diminished, the Jacksonian convulsions ceased on the third day after the operation, and the choked disks and headache disappeared. Seven weeks had elapsed since the operation at the time of presentation. A later report of this case states that the improvement lasted several months and then the symptoms returned rapidly and death soon resulted. The entire right cerebral hemisphere was replaced by a gliosarcoma.

Decompressive trephining, a term employed by Jaboulay,[4] performed for brain tumor, according to this author, has proven to be of some benefit, more often not. When done for the relief of inoperable tumors the results are not always brilliant. He speaks of astonishing results produced by trephining in the cerebellar fossa in a case of basal tumor; the pain ceased and the vision improved. The patient lived four and a half months after the operation. Jaboulay seems to believe that the relief in palliative operations is greater for tumors of the cerebellum and adjoining parts than for tumors of the cerebrum.

[1] Neurolog. Centbl., 1895, p. 472.
[2] Wien. med. Woch., 1895.
[3] Neurolog. Centbl., 1895, p. 702, and 1898, p. 974.
[4] Lyon Médical, 1896, p. 73.

Broca and Maubrac[1] ascribe to Horsley the honor of being the first to describe carefully trephining as a palliative operation in brain tumor, although scattered references to the subject are found in the literature, and they refer to Annandale and Lister. Horsley recommended making a large opening in the skull without opening the dura. Sahli, they say, recommended excision of the hernia that is produced by opening the dura, especially as the portion of the brain involved in the hernia is impaired in its function. They say that Kocher did operate in this way on a child in the service of Sahli for a tumor not localized, but probably in the cerebellum. A hernia of the cerebellum was excised and benefit resulted. Broca and Maubrac employ the term "cerebral decompression." The palliative operation, they think, exposes the patient to the danger of shock, and when the operation is performed at an advanced period of the disease death is not exceptional. When the patient survives the most distressing symptoms are lessened or disappear entirely, and, therefore, the palliative operation should be employed. It does not cause more rapid growth of the tumor. Exploratory trephining, when the diagnosis of location has been incorrect, has taught us that cerebral decompression may give important results. These authors express themselves in favor of partial removal of a tumor when the whole cannot be excised, but are undecided as regards Horsley's view that partial ablation may retard the growth of the remaining portion. They report two cases of tumor in which palliative operation was beneficial.

In 1895, J. J. Putnam[2] remarked that he knew of one patient who, in consequence of simple opening of the skull, had been free from pain for many years, though blind. He said he had seen relief from pain by large openings in the bone in several cases. He was speaking of brain tumors.

Schultze's[3] results from palliative operation in brain tumor were disappointing as recorded in his paper published in 1896. He speaks of it as often dangerous, but at times beneficial.

Ludwig Bruns[4] thinks that when the tumor cannot be removed or only a small part of it is removable, trephining does not affect the focal symptoms, but causes the general symptoms quickly to disappear if the opening is large. Consciousness returns, headache, vomiting, and choked disks disappear. In two of his cases the patients, who had hovered between life and death, had been able to walk again after palliative operations. In one of his cases (glioma of the occipital lobe) improvement lasted several months; in a second case it lasted some weeks. As headache in many cases

[1] Arch. Gén. de Médecine, February, 1896, p. 129.
[2] Boston Medical and Surgical Journal, January 16, 1896, p. 66.
[3] Deuts. Zeit. f. Nervenhlk., 1897, vol. ix, p. 217.
[4] "Die Geschwülste des Nervensystems." S. Karger, Berlin, 1897, p. 229.

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does not return at all the recurrence of symptoms is not so distressing and the patient passes into coma. The tumor, by growing through the opening, removes the pressure on the lymph tracts within the skull. Bruns says the opening in the skull must not be too small, and the dura also must be opened.

Clarke and Morton[1] report a case of tumor of the brain without localizing symptoms, in which a large area of the skull was removed for relief of intracranial pressure and the dura was not incised. Headache disappeared. They remarked that Beevor and Ballance thought that removal of bone alone without incision of the dura was not likely to relieve intracranial pressure, but they (Clarke and Morton) believe that the actual increase in the bulk of the cranial contents may not be considerable if the tumor is small, and the bulging of the dura mater even to a very limited extent may be sufficient to relieve the increase of the intracranial pressure caused thereby. Clinical evidence in Caton and Paul's case, as in their own, showed distinctly that removal of an area of bone alone is sometimes sufficient. Except for the recurrence of fits five months after the operation, the trephining was of great benefit in Clarke and Morton's case. Optic neuritis subsided, leaving some consecutive atrophy, but the patient had good vision, was entirely free from headache and vomiting, except once during the last series of fits, had recovered his mental powers and had a comfortable existence.

Alfred Wiener[2] reports a case of irremovable tumor. After opening the skull, headache and convulsions disappeared for about two months, but the tumor grew through the opening of the skull, attained considerable size on the outside of the skull, and the symptoms returned. Wiener speaks in favor of trephining in cases of brain tumor, even when there is no other hope of success than the relief of the general symptoms.

Rohmer[3] has collected a large number of cases in which the palliative operation in tumor of the brain had a beneficial effect on vision.

von Bergmann[4] has called attention to the fact that in contrast to those cases in which improvement was pronounced after palliative operations for brain tumor others are recorded in which no benefit was obtained, and, indeed, the symptoms were made worse. The improvement is only temporary and in some cases has been of very short duration. The operation also is dangerous. Improvement has occurred after merely opening the skull or after opening the dura also; surgeons, therefore, he said, preferred to remove a large piece of bone and leave the dura intact, but as cerebrospinal fluid can escape only after the dura is opened, the incision of the dura is a necessary part of the palliative operation. There was a tendency, he said, to stop at a palliative operation, and this must be strongly combated. The future of the surgical treatment of brain tumors lies in the advancement of diagnosis, and in this way the almost thankless palliative operation may be changed to a radical cure. As the escape of cerebrospinal fluid is more important than the opening of the skull, v. Bergmann recommended lumbar puncture. Since v. Bergmann wrote his book experience has shown that lumbar puncture in cases of brain tumor may be dangerous. He has been pessimistic both as regards palliative and radical operations for brain tumor. He gives a long list of cases in which exploratory and palliative operations were done, but almost all of these were attempts at removal of a tumor. In his book (1899) occurs the expression, "decompressive trepanation." He refers to a case reported by Remsden in 1825, in which trephining was done for headache.

Sänger,[1] in 1894, reported two cases to show that under certain circumstances trephining is proper, even when a tumor cannot be removed. In 1899 he presented a case of brain tumor in which a palliative operation had been performed. Inunctions were at first effective, but later the symptoms became very severe. An opening was made over the cerebellum and the cerebellar lobe at once protruded; when the dura was incised much cerebrospinal fluid escaped into the bandages for more than three weeks. After the operation vomiting and headache ceased and full recovery seemed possible. Choked disk disappeared, and vision improved so much that the patient was again able to read. The gait also improved and ataxia became hardly noticeable. The operation was performed August 7, 1899, and the presentation of the patient was made November 14, 1899.

Babinski,[2] in 1901, reported a case in which a tumor could not be found after the cerebral dura was opened, although the symptoms had been so severe as to make an operation desirable. The headache and vomiting ceased after the operation, which was performed January 14. The choked disks disappeared by January 30. The presentation of the case was made February 7, 1901. In another case Babinski observed signs of an intracranial disease. The patient had an intermittent discharge of cerebrospinal fluid by the nose. Headache was lessened by the escape of fluid and became more intense when the flow ceased. Nature in this way produced decompression he says. This case is not unlike some others reported in the literature in which Nature has effected a means of relief for intense intracranial pressure, and bears a resemblance to a case observed by me in consultation with Dr. Laplace and reported in this paper (Case 1).

[1] Brit. Med. Jour., 1896, p. 802.
[2] New York Med. Jour., Oct. 15, 1898, p. 541.
[3] Revue Méd. de l'Est., 1898, p. 525.
[4] "Die Chir. Behandlung von Hirnkrankheiten," Berlin, 1899.

[1] Neurolog. Centbl., Dec. 1, 1899, p. 1118.
[2] Revue Neurolog., 1901, p. 266.

A. Sänger[1] presented a case in which he had made the diagnosis of cerebellar tumor and an opening was made over the left cerebellar lobe. The improvement was marked, and Sänger believed that either the tumor had undergone a retrograde change or the condition was hydrocephalus. Of eleven cases in which a palliative operation was performed the symptoms were much lessened in ten. The time for operation that Sänger chooses is the beginning of impaired vision. When the opening is made over the cerebellum the dura must not be opened immediately.

In 30 cases of brain tumor studied by Leslie Paton[2] that were operated on, useful vision was saved in 22 and the vision was as good as before the operation in 18. It is impossible to draw conclusions regarding his cases in which a tumor was removed and those in which a palliative operation was performed. In the discussion following Paton's paper J. S. Risien Russell said he had no doubt that trephining was of great value in saving sight. He never hesitated to recommend the operation even in cases in which there was no chance of either localizing the tumor or removing it, for by relieving the intracranial pressure alone sight could be saved. His experience had been that removal of bone alone was not sufficient; it was usually necessary to open the dura in order to obtain sufficient relief of pressure to bring about a subsidence of the optic neuritis. Paton also expressed himself in favor of opening the dura, as he did not believe merely opening the skull was of much benefit. In two cases only the cranial cavity was opened, and blindness developed in both.

Codman[3] says:

"In 28 of the 36 operations the attempt at a radical removal of the tumor was made, and in the eight worse cases only was it decided to do only a palliative operation. I think we may almost say it is certain that if in no case the attempt at radical removal had been made and, instead, a simple operation for the relief of pressure had been done through an intermuscular incision over a "silent" portion of the cortex, the mortality would have been greatly diminished and the percentage of improvement been made much greater. I do not mean to say by this that radical operation in the hands of a surgeon who has made a specialty of brain work is not justifiable, but that in the hands of most of us, a simple palliative operation will be far better in the long run."

In my opinion, only one who has made a specialty of brain surgery should attempt the removal of a tumor of the brain.

J. J. Putnam[4] reports cases of palliative operation. In Case 2 marked relief from terrible headache and optic neuritis followed the making of a large trephine opening in the parietal region, and this, too, although the bone was replaced. This improvement was attributed to the escape of cerebrospinal fluid, which gushed in large quantities from the wound in the parietal dura. The tumor was a glioma of the lateral lobe of the cerebellum. In Case 3 a large tumor mass protruded through the trephine opening, pushing the skin before it. A measure of relief followed the operation. Recently, in association with Watermann, he has reported other cases. Lund[1] also has reported improvement from the palliative operation in cases of tumor of the brain.

Cushing[2] has reported recently cases in which the palliative operation has been of much benefit.

I add condensed notes of two unreported cases in which palliative operation was performed by Dr. W. W. Keen, with improvement in each.

Case 1.—Jan. 3, 1901, E. H. M., aged twenty-six years, complained of failing vision and had later several attacks of temporary blindness. Among the first symptoms were severe headache on the right side and vomiting, later the pain shifted to the left side. He was found to have extensive optic neuritis. He has a little vision now in the left eye but is blind in the right eye. He has sharp, boring pains which shoot from the upper occipital region to the back of the left ear. The patellar reflexes are exaggerated. Dr. de Schweinitz, Dec. 17, 1900, found optic neuritis passing into atrophy.

Dr. Keen, Jan. 30, 1901, made an osteoplastic flap over the left parieto-occipital region. The dura was very tense. Four small openings were made in the dura, but nothing abnormal was discovered. The brain was punctured in the attempt to reach the lateral ventricle, and the attempt probably was not successful. The piece of bone was removed entirely. The patient was discharged February 18, almost entirely relieved of his headache.

At Dr. Keen's suggestion, I made inquiries regarding the present condition of this man and received the following letter, dated April 20, 1906: "I am wonderfully improved and relieved as to pain, cannot see except to distinguish between night and day, have not been bedfast for a year or more, at intervals have severe pain, say every week or two, lasting from twelve to twenty-four hours, after which brain is very sore. Since last July have been having a discharge from the left nostril of a watery-like fluid, since then the pain has not been quite so severe."

Case 2.—Feb. 5, 1903. E. B., aged thirty-seven years. During the summer of 1894 a small tumor developed in the scalp on the posterior portion of the right parietal bone, producing headache and a sensation of pressure. In the summer of 1895 this mass was removed. His physician stated that it was a fatty tumor. All the pain and pressure symptoms disappeared and he was perfectly well.

After several months the headache and pressure sensation gradually returned; simultaneously with the onset of the headache his eyesight began to fail, and for the last two months he has been partly blind. He has had frequent vomiting, but he attributes this to the iodides. Ataxia was noticed in the finger-to-nose test. His gait is ataxic with a tendency to fall to the right. Lateral movements of the eyeballs are ataxic. Patellar reflexes are minus. Dr. Sweet found papillitis passing into optic atrophy in both eyes.

Feb. 11, 1903, Dr. Keen exposed the cerebellum over nearly one-half of the right half of the occipital bone. The dura was extremely tense on palpation. The patient was discharged ten days after the operation entirely relieved of his headache and with the wound healed.

[1] Verhandl. d. Deuts. Gesell. f. Chir., 1902, p. 158.

[2] Transactions of the Ophthalmological Society of the United Kingdom, 1904–1905, vol. xxv, p. 129.

[3] Boston Medical and Surgical Journal, July 20, 1905, p. 74.

[4] Boston Med. and Surg. Jour., July 20, 1905, p. 76; also Jour. of Nerv. and Ment. Dis., May, 1906.

[1] Boston Med. and Surg. Jour., July 20, 1905, p. 81.

[2] Surgery, Gynecology and Obstetrics, 1905, vol. i, p. 297.

Dr. John T. Howell wrote to me, April 23, 1906, that the patient died in a hospital in England, July, 1901, after an operation in February of the same year. The skull was opened above the ear and a large tumor was taken from the brain. After returning from the Jefferson Hospital, in 1903, the patient's improvement was of short duration.

WHEN PALLIATIVE OPERATIONS ARE ADVISABLE.

After a careful study of these cases and of the views of the different authors, it will be seen that the weight of opinion is decidedly in favor of palliative operations. The choked disk, headache, vertigo, nausea, vomiting, and, to some extent, the convulsions are all favorably influenced by this method of treatment. Relief from these distressing symptoms is by no means to be despised, even though the tumor is not removable. The relief from many of these symptoms is often permanent, *i. e.*, during the period the patient may continue to live, and, as the growth of the tumor is not hastened by the palliative operation and may be slow, we are thankful for a means of removing the distressing symptoms of intense intracranial pressure.

My first case of palliative operation was in 1898, and the operation was performed by Dr. John B. Roberts. The marked improvement that occurred in that case and persisted at least during several years and until the patient passed from our observation convinced me of the benefit to be derived from palliative operations (Case 2 of our series). She is still living and is in good health.

In one of our cases (Case 10) headache was so severe that relief was demanded at once. Byrom Bramwell, as already mentioned, has attributed sudden death in some cases of brain tumor to the severity of the headache and sudden inhibition of the action of the heart. The patient to whom I refer suffered such intense pain that he could not be reasoned with and was not responsible for his acts. Occasionally, in his attacks of pain, he grabbed anyone who might come within his reach and once bit his mother through the arm. The relief afforded in this case by a palliative operation has been most striking. Indeed, his relief from the previously constant pain has been so great that, as he expresses it, he is "lonesome without his headache."

In another case (Case 11) headache has been the symptom that above all others demanded treatment and the pain in the head was associated with pain in the neck, shooting down into the upper limbs. The symptom-complex has been in large degree that of cerebellar tumor, but the pain shooting into the upper limbs has made me fear that the tumor was extending downward through the foramen magnum on the cord. Some years ago I had a case of this kind, and at the necropsy a flat tumor was found covering a part of the pons extending into the posterior part of the fourth ventricle and growing down on the cord for several inches. In that case the development of the symptoms in the upper and lower limbs was more rapid than in the present instance, and, therefore, I feel that the tumor in the latter case may be confined to the region of the cerebellum. If so, I have no explanation for the pain in the upper limbs. The decrease of this pain, together with the decrease of the headache after the dura was opened at the second operation, gives me reason to believe that probably this pain of the limbs was indirectly caused by the cerebellar tumor. Headache and pain in the upper limbs still occur occasionally, but the condition of the patient has been vastly improved by the removal of a piece of bone and by opening the dura over the cerebellum.

I am somewhat skeptical as regards disappearance of Jacksonian convulsions after merely opening the skull and dura if the convulsions are very frequent.

In one of my cases in which the brain was exposed by Dr. Edward Martin and which will be reported by Dr. Martin and myself later, the tumor could not be found at the time of operation. The man was having five or six Jacksonian convulsions within an hour, and relief of intracranial pressure did not in any way check them. He died from exhaustion following the numerous convulsive seizures on the second day after the operation. After death a minute tumor was found nearly in the centre of the area exposed, but a little subcortical.

In a still more recent case under my care, in which fracture of the skull and subdural hemorrhage had occurred, trephining probably prolonged life about twenty-four hours, but did not in any way check the Jacksonian convulsions which before the operation were as frequent as six or seven within an hour, and continued in weakened intensity but with equal frequency after the operation. Opening the skull does not seem to relieve acute irritation of the brain, but it is of benefit in chronic cases, as not rarely convulsions occurring infrequently have been rendered less severe by this procedure.

I have considered whether palliative operations can obscure focal symptoms. Bruns thinks they cannot, but the subject is one that has important bearings. It is probable that a small tumor will cause more local disturbance if the general intracranial pressure is increased, not only because the local disturbance is added to the general pressure, but also because any one part of the brain is more irritable when the disturbance of the brain is general. This, however, is not sufficiently important to prevent palliative operation, and I would advise that this should be done before the general symptoms become very intense, and especially before optic neuritis has developed so far that blindness is likely to result. The apparent unanimity of opinion as regards the effect on choked disks of opening the skull makes the necessity of this operation at an early period very evident.

It is a mistake to regard palliative operations as a substitute for radical operations. The tumor should be removed whenever this is possible, and palliative measures are to be considered only when the tumor cannot be located, or is too large for removal, or possibly is a glioma. Palliative operations only relieve, except in extraordinary cases such as those reported by Horsley. Codman's views that palliative operations are preferable to radical operations I cannot share, and would add that the argument he offers is insufficient, viz., that the former are less dangerous in the hands of inexperienced surgeons. No surgeon who has had little experience in operating on the brain should attempt the removal of a brain tumor, and before advising the attempted removal of a brain tumor I always inquire who is to perform the operation.

The experience of Horsley as regards atrophy of tumors as a result of palliative operations seems to be unique; at least I have found no other similar cases, nor have I ever seen any such result in any of our cases. Broca and Maubrac doubted whether Horsley was correct in believing that partial ablation of a tumor may retard the growth of the rest, but Horsley has observed atrophy of a tumor following a simple opening of the skull and dura. This is a striking statement. I have never seen arrest in the growth of a tumor following the removal of a part, but several times I have seen increase of symptoms result, and I dread the partial removal of a growth, especially if it is a glioma. It has seemed to me that the congestion of the tumor and of the surrounding tissue and the greater space afforded for the growth of the tumor, after partial removal, favor the rapid growth of the remaining portion. I am almost convinced that it is better to leave a tumor untouched if only a part can be removed, especially if the growth is a glioma. The attempt, I think, should never be made to remove a glioma, and yet there seems to be no way to determine before operation that the tumor is a glioma. A patient has been under our care with the diagnosis of brain tumor and was operated on several times by Dr. Frazier. Each time as much of the tumor as could be seen was removed, and yet a return of the symptoms occurred soon after each operation, and when a necropsy was obtained the tumor (a glioma) was found to extend from the upper to the lower surface of one cerebral hemisphere.

I doubt whether it can be held that a palliative operation, by which the tumor is not partially removed, by relieving pressure, favors the growth of an intracranial tumor. Unquestionably the brain has protruded through the opening as in the cases of Schlesinger, Frazier, and Cushing, but it seems a questionable proceeding to excise the protruding portion. The tumor has grown through the opening and on the outside of the skull (Jolly, Wiener, Putnam, and others). In Jolly's case it formed an extracranial mass nearly as large as the man's head. It seems unquestionable that life was prolonged in this case by the operation, although it is doubtful if life under such circumstances is worth having. In Jolly's[1] case the clinical signs extended over a period of thirteen years. In the case that Dr. Martin and I observed, to which reference has been made, the symptoms of brain tumor had existed for eight years.

We have had some extraordinary cases in which the symptoms of brain tumor disappeared entirely or almost entirely after an opening had been made in the skull and dura; such, for example, is the case observed by Dr. John B. Roberts and myself in 1898, and also Cases 4, 5, 6, 9, 10, of our series. It may be thought that the growth of the tumor is arrested by the operation; this is possible, but doubtful. Internal hydrocephalus (meningitis serosa) or some other lesion may give the symptoms of brain tumor, and relief of intracranial pressure may cause great modification or disappearance of the symptoms. In some cases in which relief has followed palliative operations probably an incorrect diagnosis has been made; in others, the relief of pressure has permitted the tumor to grow slowly without causing many symptoms. My views as a result of my experience and of a study of the literature are:

1. Palliative operations should be performed early in every case in which symptoms of brain tumor are pronounced and before optic neuritis has advanced far, especially when syphilis is improbable or antisyphilitic treatment has been employed.

2. Partial removal of a tumor, especially of a glioma, is a questionable procedure.

3. Palliative operation does not under ordinary circumstances cause atrophy of a brain tumor and probably does not arrest its growth; on the other hand, it probably does not hasten its growth.

4. Palliative operation is not to take the place of a radical operation when the latter can be performed without great risk to the patient.

5. In some cases the symptoms of brain tumor disappear almost entirely for a long time or permanently after a palliative operation. This result is obtained either by relief of intracranial pressure or by removal of some lesion (meningitis serosa, etc.) other than brain tumor, and yet causing the symptoms of tumor.

REMARKS BY DR. FRAZIER.

The question as to whether a palliative or radical operation is indicated may be determined by answering the question as to whether the tumor is operable or not. The operability of brain tumors has frequently been discussed and the facts and figures which have been presented to us have been based

[1] Berl. klin. Wochft., July 17, 1899, p. 636.

almost exclusively on the autopsy records and not on the finding at the time the operation was performed. The autopsy records may help to determine the percentage of operable tumors in so far as it reveals the nature of the tumor and may be able to fix on its point of origin. The very vascular infiltrating sarcomata should be classed with the inoperable tumors, for I believe the expectation of life and the enjoyment of that much of life which remains to the patient would be greater in the majority of cases after a palliative operation. On the other hand, the fibroma, or the somewhat defined fibrosarcoma and the gumma of limited dimensions, should be classified as of the operable group. The size of the tumor as revealed at the autopsy has no practical bearing at all on the problem; the size of the tumor at the time the symptoms first made a diagnosis possible should only be considered. There are some tumors of such large proportion as to make any attempt at removal inadvisable, but, on the other hand, tumors of very small dimensions may lead to a fatal termination.

If it were possible to ascertain the point from which the tumor took its origin we should have some valuable statistics as to the operability of tumors. The further away the tumor is from the cortex or the nearer it is to the base of the brain the more it approaches the field of inoperable growth If the statistics are to be of much value to the surgeon they should be based on the records which are made on the operating table or at the autopsy, if the patient dies as a result of operation, only in those cases in which the patient has been brought to the surgeon comparatively early in the course of the disease. One might as well prepare a table and compile statistics as to the operability of carcinoma of the stomach based on the autopsy records of patients who died in the most advanced stages of the disease, when the lymphatic nodes far beyond the primary lesion have been invaded and the tumor is no longer confined to the stomach, but has invaded other organs adjacent to it. The question as to what percentage of tumors of the stomach may be removed must be and is being determined in the very earliest stages and on the operating table. So with tumors of the brain, the greater the number of cases brought to the surgeon in the earliest recognizable stage of the disease the sooner will we be able to say with some degree of accuracy in what percentage of cases there is a reasonable hope of being able to perform a radical operation.

There are two classes of cases in which a decompressive operation may be required. One in which there is reason to believe the tumor cannot be removed in its entirety and the other in which the tumor cannot be localized and yet the possible loss of vision, the intense headache and distressing vomiting almost demand the immediate adoption of some measure of relief.

Cases of tumors of the cerebrum in which localization is impossible are rather the exception, although in cerebellar lesions it not infrequently happens that the tumor cannot be localized.

A word or two might be said with reference to operations performed for the relief of cerebellar tumors. The anatomic relations of the structure in the suboccipital resemble in certain particulars those in the temporal region. In both the bone is covered with a well-developed musculo-aponeurotic layer, even of a greater bulk in the suboccipital than in the temporal region. For purposes of exploration it is necessary to reflect a flap of considerable size, the incision beginning at the mastoid process and following the line of the transverse sinus to the occipital protuberance, drops in a vertical direction along the median line. And when the flap is replaced great pains should be taken to approximate carefully not only the cutaneous, but the musculo-aponeurotic layer. When the tumor cannot be localized or for any other reason a radical operation is not deemed feasible a less mutilating incision will answer the purpose quite as well. A vertical incision should be made, beginning a little above the superior curve line and extending downward for a distance of three or four inches. The edges of the wound can be retracted sufficiently to afford space necessary to carry on the subsequent steps of the operation. A much more perfect approximation of the wound may be obtained as the muscles are split in the direction of their fibres and not in various angles, as is the case when a curved incision is made following the line of the sinus. This vertical incision enables one to remove the bone only from one side, but if for any reason a bilateral craniectomy seems advisable, the muscle-splitting operation may be repeated on the opposite side. Such a procedure has many advantages over the conventional bilateral craniectomy in which the bone from one mastoid process to the other is removed. There is less chance of disturbance arising from traction on the pons or medulla if an intervening bridge of bone is left. In addition to this the bone in the region of the occipital region is very vascular, often riddled with vascular channels of such dimensions as to admit of a very profuse and sometimes alarming hemorrhage. The region immediately surrounding the occipital protuberance should be regarded as the dangerous zone and as such scrupulously avoided.

Failing to find the tumor, we have in certain cerebellar cases deliberately removed from one-quarter to one-third of the cerebellar hemisphere and have attributed the relief of pressure, in part at least, to this. In all our cases the operation has been confined to one side, and as yet we have not found it necessary to operate a second time for the removal of the bone on the opposite side. Even if it were conceded to be necessary to remove eventually the bone overlying both hemispheres the operation had better be performed in two stages rather than in one; patients with cerebellar lesions are at the best not very favorable subjects for operative intervention, and

preference should be given, therefore, to this precedure, which in giving the desired results will require less time and be attended with less hemorrhage and traumatism of the tissues.

First, as to those cases in which the tumor cannot be localized. There are two points in the technique of the operation about which there may be some difference of opinion, namely, the area of the brain to be uncovered and the incision of the dura. The decompressive operation consists solely in the removal of a portion of the cranial vault with or without incision into or removal of a portion of the dura. When there is no guide as to the situation of the tumor the operator is free to select either one of four areas: the frontal, parietal, occipital or temporal. In discussing this question several years ago, attention was called to the desirability for cosmetic reasons of avoiding both the frontal and occipital regions; there remain, therefore, but two areas from which to make the election: the parietal and the temporal. It is desirable, as Sänger suggests, to give preference to that portion of the skull beneath which may be said to exist a silent area of the brain. This is especially true of the right temporal region, so that, in the absence of any contraindication, this may be said to be the region of choice. Through a longitudinal incision, following the direction of the fibres of the temporal muscle, a section of bone equivalent to 6 or 8 square centimetres may be removed. One should be content to make but one opening, at least at the first sitting. This will be found in most cases to be sufficient to afford the necessary relief of pressure. If in the course of events there is evidence of a recurrence of increased tension, as shown by such symptoms as headache, vomiting or choked disk, a second opening may be made on the opposite side of the head. Such were the circumstances in one of our patients (Case 5). The headache, which had been relieved temporarily, recurred. A second opening was made on the opposite side of the head, and since that time, a period of about three years, the patient has enjoyed almost entire relief.

Speaking now only of those cases in which the tumor has been definitely localized, it is impossible to determine prior to the operation whether the tumor is one appropriate for a radical rather than a palliative operation. The duration of the disease is a guide neither to the size nor to the nature of the tumor. Malignant tumors in the brain are many of them surprisingly slow in their growth, and, though of many months' or years' duration, may still be in the operable stage. A very large tumor may be present with comparatively slight disturbance, or a very small one may be very serious in its consequences. A tumor of several years' duration may be no larger than a hickery nut or walnut, and yet give rise to a condition which may ultimately prove fatal.

Recently I was called by Dr. Charles K. Mills to operate on a patient who had had symptoms of a tumor for more than a year. The localizing symptoms were very vague, but all seemed to point to a lesion of the left cerebellar hemisphere. This was thoroughly explored, but with negative results, except in so far that there seemed to be a very unusual degree of tension within the cerebellar fossa. This was so suggestive of the presence of a tumor as to justify a very careful search. The results were negative. About two weeks later the patient died, and a tumor as large as a peach was found compressing the under part of the occipital lobe directly in contact with the tentorium cerebelli. Its position satisfactorily explained the existence of cerebellar symptoms. As the brain was being lifted out of the cranium at the autopsy the tumor dropped on the table. Though of large dimensions it was clearly an operable one, and had the symptoms made it possible to localize the growth it could have been removed without any difficulty, and owing to its benign nature the operation would have resulted in a complete cure. In such a case had the operator proceeded deliberately to the performance of a decompressive operation and not attempted to explore the affected area the opportunity of saving the patient's life and of affording him permanent relief would have been thrown away.

In every instance, therefore, the operator should begin the operation with the intention, first, of attempting to expose the tumor. He should proceed as for the performance of an osteoplastic operation; the flap should be carefully mapped out and reflected and the usual exploratory measures adopted. Failing to find the growth or finding an inoperable one, the propriety of a decompressive operation is clearly indicated. He must then determine as to whether he will remove the bone of the flap, wherever this may be, or close the flap and remove the bone from the area of choice, namely, over the right temporal lobe. When, as is true in the majority of cases, the tumor is situated in the postfrontal (motor) or parietal region the bone over the temporal region may be removed through the same opening, thus avoiding the necessity of another incision. This was the procedure adopted in one of our reported cases. The patient was suffering so intensely from headache that he was operated on the day of his admission to the hospital; not waiting to make a more careful study of the case with a view toward accurately localizing the growth, we proceeded at once with the intention of performing a decompressive operation. Sufficient was known of the case to lead us to believe the tumor was in the motor region. Accordingly this was laid bare and a very large vascular tumor, probably a sarcoma, was at once exposed. Deeming it to be inoperable and wishing to afford relief from the intracranial tension, only the lower half of the bone contained in the flap, which extended down to the Sylvian fissure, was removed, but through the same opening a considerable portion of the bone lying below the fissure and under the temporal muscle was also removed with rongeur forceps. As will be seen in the record (Case 10) the headache was immediately relieved.

The most important question, however, in the technique of the decompressive operation is as to whether the dura shall be incised or removed. The region from which the bone is to be removed is by comparison a matter of slight importance. To be able to answer this question one must be in a position to state from experience, first, whether the escape of cerebrospinal fluid through a dural opening is essential, and secondly, whether sufficient relief of tension may be afforded with the dura intact. As to the escape of cerebrospinal fluid there are certain observers, notably v. Bergmann, who believe that the beneficial effect of this operation is largely attributable to the escape of cerebrospinal fluid. It might

Fig. 1.—Showing the protrusion subsequent to the development of a hernia cerebri following a decompressive operation, in which, after exploration, the dural wound was closed.

be difficult, possibly, to prove or disprove this idea on theoretical grounds, but from our own experience we have not been able to note any radical difference in the results between those cases in which the dura was either left intact or if incised or exploration was closed immediately afterward. To the escape of a small quantity of cerebrospinal fluid through a temporary opening in the dura could scarcely be attributed the relief, which extends over a period of months or years. In so far, therefore, as the results of the operation are concerned, it makes no difference whether the opportunity for drainage was afforded by a permanent opening in the dura. In the most satisfactory of the cases under our care the dura was closed; in one case, particularly, in which an exploratory dural incision was not entirely closed, the patient enjoyed no appreciable benefits from the operation.

I think it is very generally believed by those who have had but little experience with these operations that the success of the operation depends on the establishment of an opening in the dura as well as in the skull. It is said that the dura is not elastic enough to stretch sufficiently when subjected to pressure. That the dura will stretch, when the overlying bone is removed, sufficiently to afford adequate relief of tension has been demonstrated in our cases over and over again. Take, for example, a case which was operated on for a tumor

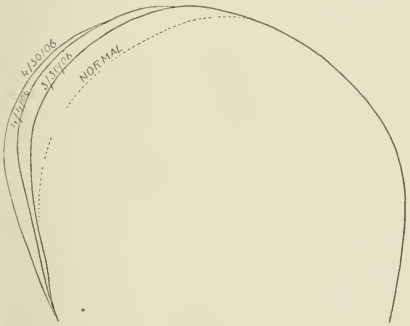

Fig. 2.—Showing the rapid development of a hernia cerebri in the decompressive operation. After the operation the dural wound was closed. The dotted line represents the normal contour on the affected side. The other lines represent the contour of the head: (1) March 30, 1906, one week after the operation. (2) April 4, 1906, twelve days after the operation. (3) April 30, 1906, five weeks after the operation.

believed to be in the occipital region. The tumor was not to be seen on or near the cortex, but there was a very much dilated right ventricle, possibly due to a tumor at the base, cutting off the intraventricular communication. If we turn to the illustration (Fig. 1) we see a genuine hernia cerebri, a hernia in which the dura as well as the scalp form the coverings. This patient has been under observation for a number of years and for the past year the hernia has not increased in size. The optic neuritis was in this case too far advanced to enable us to save the patient's vision: in other respects the patient enjoys excellent health and is now in attendance at an educational institution. A decompressive operation was

not a matter of choice in this case; at least at the outset this was not contemplated. The brain bulged so through the opening that it was impossible to close the flap without removing the bone.

As an example of how rapidly the dura may stretch when subjected to excessive pressure, one of the cases of our series may be cited in which an exploratory craniotomy revealed a large and very vascular ill-defined sarcoma. Its removal was out of the question; the incision in the dura was closed and a section of bone removed. Several records were made of the convexity of the head (Fig. 2) at short intervals, and it is rather surprising to find how rapidly the dura had expanded to accommodate the growth. On the other hand in another case in which a tumor was exposed and found inoperable the dural incision was only partially closed. The results in this case were as compared with the other, in so far as the relief of symptoms was concerned, much less satisfactory.

Whatever else may be said either in favor of or against the removal of the dura it should be borne in mind that if the dura is removed and any complication arises in the repair of the wound it is more than likely that a fungus cerebri will develop. An accidental wound infection, the persistence of a sinus, the remains of a drainage tract may result in infection of the exposed brain tissue and that very fatal condition a fungus cerebri. In the hands of operators experienced in this field of surgery the danger is very slight, but it is questionable whether the removal of the dura should be resorted to as a universal practice. While in a given number of cases the results may not be so pronounced the mortality will be higher unquestionably if the dura is removed in every case. Inasmuch as the brain may herniate through the opening in the skull when the dura is left intact, there is really no necessity for removing more than the overlying bone. If the dura is disturbed at all, the operator should be content with making a crucial or radiating incision in it, and in many cases it may be advisable to reserve this step of the operation until indications arise for further intervention. This course was pursued in one of our cerebellar cases in which temporary relief having been afforded the symptoms, particularly pain, recurred.

A muscle-splitting incision was made, the edges of the wound retracted and a crucial incision made in the dura. The results were very gratifying and have continued so now for a period of several months.

Mortality. Every one of the twelve patients operated on at the University Hospital, eleven by Dr. Frazier and one by Dr. Martin, recovered. The absence of any fatalities in the entire series is worthy of note. When one is debating as to the advisability in a given case of performing a radical or palliative operation, consideration should be given to the fact that there is at least no immediate risk as to life from the decompressive operation. In the palliative measure we have an operation which almost inevitably relieves the sources of discomfort and suffering, not only without endangering but frequently prolonging life; in the radical measure we are undertaking an operation, which has a comparatively high mortality and is only successful in a small percentage of cases in finding and removing the tumor.

Results. The opinions expressed in the paper are based on observations in a series of fourteen cases. The first operation was performed in 1898 and the last March 20, 1906. In but one of the entire series did the operation fail to afford the relief which would justify its performance. There was in this case some immediate improvement, but so slight as not to warrant the promise of relief which was held out to the physician and relatives of the patient. The operation was performed in March of this year; the patient was at the time almost comatose and her life was in immediate danger. At the present writing, May 25, 1906, her physican, Dr. Thomas O. Nock, writes me that the patient has been moved to the country, but her condition is little, if any, improved. All that can be said of this case is that life has been prolonged. The results in this case are a striking contrast to those following an operation performed in October, 1903. This patient probably has two lesions, one in the parietal lobe and one in the cerebellum, and before the operation suffered intensely from headache and neuralgia. When last heard from two and a half years after the operation she still enjoyed absolute relief. Perhaps the most brilliant of the series was a patient who presented the clinical symptoms of a cerebellar lesion, intense choked disk, frightful headaches, and persistent nausea, vomiting and ataxia. This patient (Case 4) was operated on two and one-half years ago and when last seen, February of the present year, he was the picture of health and was engaged in hard manual labor. Neither headache nor nausea recurred, and though he had a choked disk, so elevated that he could scarcely recognize large objects, his vision is now practically normal. Apart from the fact that he occasionally has attacks of what he calls "dizzy spells" he is to all intents perfectly well and now weighs 184 pounds.

The decompressive operation offers to the patient relief from the three cardinal symptoms of cerebral tumor, headache, nausea, and vomiting, restores vision, and if the lesion is in the cerebellar fossa relieves ataxia and vertigo. Mention has already been made of the dangers of postponing operation once there are signs of choked disk. One of the strongest arguments in favor of the palliative operation is the opportunity to save or restore the patient's eyesight. Without exception the choked disks subsided in every instance but unfortunately in at least three of our cases the patients remained totally and hopelessly blind because the optic neuritis was of so long duration that the nerve had undergone atrophy. The subsidence of the choked disk takes place as rapidly when the dura is left intact as when it was

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incised. The case, which in Dr. de Schweinitz's opinion and experience responded most promptly to the operation, was one in which the dura was not disturbed. Although the operation was performed only seven months ago the patient's vision has continued to improve. The prospects of preserving the eyesight alone would justify the operation, but no less so the opportunity of relieving headache. Our results with respect to headache have been uniformly good. There were two or three cases in which the headaches did not entirely cease, but in these there were intervals of relief and the headaches were less severe. As to the duration of the period of relief the longest in our series is between two and one-half and three years. In at least three of our cases the intensity of the pain seemed to be as great as that of a tic douloureux, and one patient had become addicted to the liberal use of morphine; yet in each one of these the relief was immediate, absolute, and permanent. In one instance the suffering was so intense that the operation was performed within a few hours of the patient's admission to the hospital, before an opportunity was afforded to determine with any degree of accuracy the location of the tumor. What has been said of the beneficial effect of the operation on the choked disk, even when the dura was left intact, may be repeated in dealing with headache. Not that the dura was not opened in some cases for exploration, but in almost every instance the dural wound was immediately closed with sutures.

Mention might be made of the fact that in two instances Nature had already begun to relieve the intracranial tension. In these cases the tumor had grown through the dura and in one instance had almost perforated the skull. In conclusion we may say that there is no form of treatment, either medical or surgical, which, in the presence of an incurable lesion, causing sometimes great discomfort, sometimes intense suffering, so uniformly affords so great and enduring a measure of relief.

SUMMARY OF CASES.[1]

	Location of lesion.	Period since operation.	Results.
1. L.	Cerebrum	1 year (operation was not performed but relief of pressure occurred spontaneously).	Alive and free from palu.
2. B.	Cerebellum	7 years.	Almost complete recovery during two or three years; present condition unknown.
3. G.	Cerebellum and cerebrum	2 years and 7 months.	Alive and free from pain.
4. E.	Cerebellum	$2\frac{1}{2}$ years.	Alive and free from pain.
5. D.	Cerebellum	$2\frac{1}{2}$ years.	Alive and free from pain.
6. B.	Cerebrum	1 year and 7 months.	Alive and free from pain.
7. M.	Cerebellum	8 months.	Second operation was performed; tumor found and removed.
8. K.	Cerebellum	7 months.	Died seven months after operation.
9. L.	Cerebellum	7 months.	Alive and free from pain.
10. S.	Cerebrum	$2\frac{1}{2}$ months.	Alive and free from pain.
11. F.	Cerebellum	$2\frac{1}{2}$ months.	Alive and free from pain.
12. D.	Cerebellum	2 months.	Radical operation was performed two months after palliative operation.
13. C.	Cerebrum	.....	Alive but little if any relieved.
14. S.	Cerebellum	About 3 years.	Improved; death from tumor about three years after palliative operation.

[1] A case under the care of Drs. Spiller and Martin to which reference is made in this paper, is not included in this table.

ORIGINAL OBSERVATIONS.

CASE 1.—Probably tumor of motor area. The following case is of great interest as it seems to be one in which relief of symptoms from intracranial pressure occurred by escape of cerebrospinal fluid through the cribriform plate of the ethmoid bone without operation, and it may be, therefore, regarded as a case in which relief was afforded in a manner similar to that in palliative operations.

Examination. L. was seen by Dr. Spiller in consultation with Dr. Ernest Laplace, Aug. 13, 1904, at which time the following notes were taken: In showing the teeth the left corner of the mouth is drawn up better than the right. When drawing up each corner of the mouth separately he draws up the left better than the right. The eyelids are closed equally well on the two sides, and the resistance to any attempt to passively open the lids is as good on one side as on the other. Percussion of the scalp shows no area of tenderness. When the tongue is protruded it tends to deviate a very little toward the right. The movements of the tongue are free in all directions, and the tongue is not atrophied. The movements of the eyeballs seem to be normal in all directions, except that the movement to the left may be a trifle impaired. There is no nystagmus. The reaction of the iris to light is preserved, but tardy on both sides. Convergence and accommodation cannot be tested satisfactorily on account of the mental condition. The pupils are equal and regular. The masseter muscle contracts well on each side, but the left masseter contracts a little better than the right when the patient bites. He says that he feels touch more distinctly on the left side of his face. Pin-prick is probably perceived in the right side of the face as well as in the left, but his statements regarding sensation are not to be relied on. He understands what is said to him, although he appears dazed and has difficulty in replying, but apparently is not aphasic.

Upper limbs: The grasp of the right hand is distinctly impaired and is decidedly weaker than that of the left hand. The upper limbs are well developed and equally so. The biceps and triceps tendon reflexes on the right side are distinctly prompter than the corresponding reflexes on the left side. After a spasm the right upper and right lower limbs seemed to be almost completely paralyzed, and Dr. Laplace says that this paralysis following a spasm is only temporary.

Lower limbs: The lower limbs are well developed and there is no atrophy in any part. The patellar reflex is about normal on the left side, but exaggerated on the right side. There is no ankle clonus on either side. The Achilles tendon reflex is about normal on each side, and a trifle prompter on the right than on the left. The Babinski reflex is very pronounced on the right side; the big toe as well as the adjoining toe being drawn upward distinctly. The Babinski reflex is not present on the left side, the movement being flexion.

During the examination an epileptic attack occurred. It began with a slight flexion of the right forearm on the arm. This movement lasted from thirty to sixty seconds before the face was involved. The right lower limb seemed to be involved before the face. Clonic movements of small extension began in the right lower limb, afterward the movements occurred in the right upper limb. Both right upper and lower limbs were very spastic. The right side of the face was thrown into violent tonic spasm, and the lids on both sides were equally affected. There seemed to be a slight tendency of the eyeballs to turn to the right, but this was not pronounced. The lower part of the left side of the face, the left upper and lower limbs showed no convulsive movements and the left limbs were not spastic. Consciousness did not seem to be lost during the attack. Urine was not voided during the attack, but was immediately after the attack, voluntarily. After the attack the man was drowsy and passed into a light sleep lasting about five minutes.

Further Examination. A further examination on August 14th gave the following results: Sensation for touch is more acute on the left side of the face; sensation for pain is more acute on the right side of the face; this agrees with the findings of yesterday. The grasp of

the right hand is not so good as it was at the beginning of the examination yesterday. A knife or a pencil put into the right hand is distinguished without difficulty when the eyes are closed. The weakness of the right upper limb has been much greater since the attack that we saw yesterday than at any time previously. He can barely lift the right hand from the bed. The paralysis of the right lower limb which developed after the attack that we saw yesterday disappeared in part during the afternoon, whereas, that of the right upper limb has persisted with very little change. The sensation for touch and pain seems to be more acute in the right lower limb than in the left. He seems to understand what is said to him, but has difficulty in getting words to reply and is partly motor aphasic. He yawns repeatedly and Dr. Borsch has noticed that during the convulsive attack the eyeballs are drawn toward the right but remain in this position only during a short part of the attack. The left pupil is larger than the right and the left recovers more slowly than the right.

Subsequent History. The following notes were obtained from Dr. Laplace: The patient continued to improve under high doses of iodide of sodium (100 grains daily) until all symptoms of paralysis had disappeared. Headaches also disappeared, but the optic neuritis continued. The field of vision gradually lessened until total blindness ensued, January, 1905. The patient remained in this condition until May, when convulsions attended by severe headaches returned, exactly similar to those seen by Dr. Spiller in August. About forty convulsions took place in the course of the first week in May, 1905. He suffered with intense headaches and was suddenly greatly relieved of all headache and of nearly all the other symptoms on expectorating what seemed to be a certain amount of purulent material. (Dr. Laplace did not see the patient at the time of this nasal discharge.) Whether the material contained cerebrospinal fluid or whether it was pus which found its way into the nose, after burrowing its way through the cribriform plate of the ethmoid can, therefore, only be conjectured. In June and July the patient improved, but his lower extremities remained weak. This weakness of the lower extremities has increased gradually from July, 1905, until the present time. Mental hebetude gradually set in, but there has been an absolute freedom from headache, from July, 1905, until now.

Present Condition. Complete blindness; perfect consciousness. He is thoroughly rational when aroused; otherwise quite listless. There is great weakness of lower extremities, requiring support to enable him to walk. Both arms are quite strong. Excellent appearance; good appetite and digestion; full control of bowels and bladder. Freedom from headache. Last report says that general weakness is gradually becoming more marked. Mercury and iodides have been continued. The patient and his family have opposed any surgical interference.

Case 2.—Tumor of cerebellum (?). Mrs. M.B., was admitted to the Polyclinic Hospital, Dec. 31, 1898, under the care of Dr. Spiller and Dr. Roberts.

History. Patient had been married twenty-six years, a widow, eighteen years; had two children, twenty-five and twenty years old, respectively, at time of death. Emigrated to America five years ago. She had good health until previous to present trouble. Her present condition began two and one-half years ago with violent headaches in the left occipital region. Her symptoms have gradually increased in number and intensity, until at present they consist of very severe headache in the left occipital region, great tenderness over the same region, extreme vertigo, especially when lying on the left side in bed or attempting to walk; very ataxic gait so that she staggers like a drunken person and falls to the left side or backward.

Examination. The patellar reflexes are absent; sensation in the legs is obtunded and movements of the lower extremities somewhat restricted (she cannot cross her legs). During the last few months she has been getting rapidly worse. A diagnosis of cerebellar tumor was made, and the patient was admitted to the wards of the Polyclinic Hospital for an exploratory operation. Urinary examination: color, amber; cloudy, reaction acid; specific gravity, 1020; no albumin or sugar.

Operation. On June 4, 1899, under ether, the skull was opened by trephine and lion-jawed forceps, a hole about one and one-half inches in diameter being made over the probable seat of the lesion as indicated above. The dura mater appeared normal, as did the bone removed; the dura mater was laid back, the brain exposed, the finger inserted and the surface of the brain palpated for an area of five inches or more in diameter, but no abnormality was detected. A puncture was then made into the convolutions of the brain in several directions with a grooved director to the depth of three-fourths inch without finding any lesion. The dura mater was then sutured, and the skin flap brought into place and secured. The patient made a good recovery from the anæsthetic, but her temperature began to rise rapidly that night, reaching 101° F. at 7 P.M. Infection being feared, the dressing was removed, the sutures partially withdrawn, and the wound flushed with normal salt solution. The wound was re-dressed at frequent intervals since, all the sutures removed.

Results. June 30th. The patient has been slowly improving since the 20th, the temperature having been practically normal. The parietal region on the operated side has almost entirely lost its peculiar tenderness to touch, and the headache occurs only occasionally, is slight and is now located in the frontal region. The patient made a complete surgical recovery, and almost all her symptoms disappeared. After two or three years she returned to Europe. She has been seen recently and is in good health.

Case 3.—Tumor of the pons. Mrs. G., aged forty-five years, was admitted to the University Hospital under the care of Dr. Charles K. Mills, October, 1903.

History. Tumor of the pons, probably second lesion in the parietal lobe; cyst evacuated; permanent disappearance of severe headache and facial neuralgia. This patient, a woman about forty-five years old, first came under the care of Dr. Mills in November, 1902. One year before coming under observation she had an attack of vertigo without unconsciousness and after this partial paralysis of the left third nerve was observed, ptosis, dilated pupil and paresis of the internal rectus being present, according to the physician then in attendance. From the history she also appeared to have had temporary paralysis of the left side of the face. She had subsequent similar attacks, some of these shortly before coming under observation. In one of the recent seizures she was found in the cellar, pacing up and down with her hands above her head, eyes dilated, and apparently struggling against suffocation. She was taken upstairs and put to bed; she tried to speak, moving her jaws without uttering a sound; her face was pale, her eyes were open. At the time of the first examinations she had paresis of the left side of the face, partial ptosis, pupils equal and responsive, the superior rectus not being as active on the left side as on the right.[1]

Examination. The patient was again examined by Dr. Mills and Dr. Spiller, Sept. 22, 1903. The left side of the face was paralyzed in the entire distribution of the seventh nerve. She complained of much pain, confined to the left side of the face and in the distribution of the fifth nerve. The masseter and temporal muscles contracted well in chewing on each side. No distinct objective disturbance of sensation on the left side of the face was made out. The left external rectus seemed to be the only external ocular muscle distinctly paretic. Astereognostic conception as tested in the right hand was almost complete.

She complained of much pain on both sides of the forehead, extending down the left side of the face to the lower border of the lower jaw. The pain did not extend below the median line of the lower jaw; it extended to the mastoid process, but not beyond this on the left side; it did not extend into the neck. She had constant pain in both temples, but it was greater in the left than in the right. All points of exit of the fifth nerve were painful to pressure; as much so on the

[1] The case is fully reported as Case 6 in a paper by Dr. Charles K. Mills, on "The Diagnosis of Tumors of the Cerebellum and Cerebello-pontile Angle, with Special Reference to their Surgical Removal," New York and Phila. Med. Jour., Feb. 11 and 18, 1905.

right side as on the left. Sensation for touch and for pain on the two sides of the face seemed to be normal; she felt a touch or pin-prick as well on the left side of the face as on the right. In such instances, as when chewing a hard crust of bread, the left masseter contracted, but not so well as the right; in opening the mouth the lower jaw did not deviate distinctly. She complained of a sense of numbness in the left side of the face; this involved the entire distribution of the fifth nerve and extended on the left to the temple, but not far beyond the border of the hair. There was considerable improvement in the paralysis of the orbicularis palpebrarum. There was complete paralysis in the lower distribution of the left facial nerve. The right side of the face was normal. She did not have any nausea and seldom had spells of vertigo, although formerly the latter occurred frequently. She showed at times a tendency to fall backward or toward the left, but did not stagger as much as formerly; closing the eyelids did not affect the gait very distinctly. Hemiasynergia was not present on either side.

As the patient was slowly getting worse and was suffering extremely with pain in her head and face, it was finally decided to remove her to the University Hospital for the purpose of having an operation, which might at least be palliative. Her pain increased until it became torturing, and for days before the operation it was necessary to keep her continuously under the effects of morphine or codein. No change of any movement occurred in her local symptoms after the above recorded notes.

Operation. The operation was performed by Dr. Frazier, Oct. 14, 1903, under ether anæsthesia. A musculocutaneous flap together with the periosteum was reflected and an opening was made in the skull with the chisel and enlarged with rongeur forceps. Nothing abnormal as regards pulsation nor consistency of the left lateral lobe of the cerebellum was noted. The dural flap was reflected; at one point this flap was adherent to the underlying brain. Cerebellar tissue bulged only moderately through the wound. On exploring with the index finger in the region of the cerebellopontile angle some adhesions were separated on the lateral aspect of the cerebellum. This was followed by a gush of fluid which had evidently been walled off by adhesions. After the evacuation of the cyst the bulging subsided immediately and with a brain retractor it was possible to inspect the region of the cerebellopontile angle and to demonstrate to those present at the operation, the fifth, seventh, and eighth cranial nerves. It was noted on the blood pressure chart that when the dura was opened the blood pressure dropped thirty points and that on introducing gauze packing, or on compressing the brain with the retractor that the blood pressure rose forty points. The patient's condition was not depressed to any considerable degree by the operation; on her return to bed the pulse was 145; respirations were 40, and blood pressure was 115.

The interesting feature of the case was the ease with which the cranial nerves were exposed after the cyst had been evacuated.

The patient reacted well after the operation and passed a fairly comfortable night. There was very profuse oozing of blood and cerebrospinal fluid, necessitating frequent reinforcement of dressing. The patient was much nauseated, vomiting curds of milk and bile-stained fluid. She complained of pain in her temples. An incomplete examination showed that sensation was present on both sides of the face and no inequality of pupils was noted. On October 15th, the wound was dressed and found in good condition; the drainage was removed, there was a free flow of cerebrospinal fluid.

Subsequent History. An examination by Dr. Mills and Dr. Spiller on October 15th, resulted as follows: No cutaneous anæsthesia was present on either side; not even any hypæsthesia on the left. There was no great impairment of the motor division of the fifth nerve, the masseter and pterygoid muscles being tested. Complete paralysis in the muscles supplied by both the upper and lower branches of the seventh nerve was present. She was completely deaf in the left ear.

Slight paralysis in the right upper extremity was noticed. Astereognosis or pseudoastereognosis was present in the right hand. Anæsthesia for both touch and pain and hyperæsthesia were absent. She had had no pain in the face or head since the operation and had required no anodynes.

October 19th. The wound was again dressed and the stitches were removed; the wound was healed, with the exception of one angle; a small piece of gauze was inserted for drainage. The patient's general condition had been very good. Her pupils were normal

24th. The surgical condition was entirely satisfactory; the wound was healed, with the exception of one spot, which was rapidly granulating. The patient's general condition had rapidly improved since last noted. She was regaining strength, had been sitting up and was quite comfortable.

29th. Patient was discharged, the surgical condition left nothing to be desired; the wound was completely healed; there was no bulging of the flap, no signs of inflammation or œdema of the scalp. She had not had any pain in the head or ears; the only discomfort had been some irritation of the conjunctiva of the left eye, which was probably due to facial palsy.

Results. When the patient was last heard from two years after the operation, the relief from headache and neuralgia continued, although, as previously stated, the pain for some time before the operation was of the most intense character. In other respects her general condition has been good. She still continues to be partially paralyzed, with astereognosis and sensory changes on the right side and still has paralysis in the distribution of the left seventh nerve. It is altogether probable that a lesion of some sort is still present; not improbably she has more than one lesion, as the symptoms point both to the pons and to the left parietal lobe. The case is especially interesting as showing how the cerebellopontile angle can be exposed and how pain and other symptoms of brain tumor are sometimes relieved even when full success is not obtained.

Case 4.—Tumor of the cerebellum or cerebellopontile angle. The tumor was not found, but great benefit was obtained by a craniotomy associated with excision of a portion of one lateral lobe.

History. C. E., aged twenty-three years, was admitted to the University Hospital, December 7, 1903, and was placed under the care of Dr. Charles K. Mills, who reported that his illness began several months prior to his admission to the hospital, the principal symptoms being dizziness and intense headache, starting in the occipital region and radiating toward the forehead. Five weeks later his sight began to fail and a week later some weakness of the left arm and leg were noticed.

At the time of his admission to the hospital he was suffering from the most distressing headache, which was almost constant, and from vertigo and ataxia to such an extent that it was almost impossible for him to walk alone or without support. Nor could he even stand alone unless leaning against some stationary object. His vision was so affected that he could not see gross objects and the examination of his eye-grounds revealed the presence of very marked choked disks and optic neuritis.[1]

Operation. The patient suffered so that it did not seem justifiable to postpone operation for further and more elaborate study of the case. Accordingly within a week of his admission to the hospital a left cerebellar craniectomy was performed by Dr. Frazier. The dura was noted to be unusually tense, and on reflecting the dural flap a considerable portion of the cerebellar hemisphere protruded through the opening. It was found to be almost impossible on account of the protrusion of cerebellar tissue to make further exploration, so the operator proceeded to remove from one-third to one-half of the lateral lobe. After this was accomplished, exploration was continued, but to no avail. No tumor could be seen or felt in any portion of the left cerebellar fossa.

Subsequent History. The postoperative record of this patient is one of unusual interest because of the remarkably rapid improvement

[1] This is Case 4 in Dr. Mills' paper, "The Diagnosis of Tumors of the Cerebellum and Cerebellopontile Angle, with Special Reference to Their Surgical Removal," New York and Phila. Med. Jour., Feb. 11 and 18, 1905.

which followed. Within one week of the operation the patient's headache had entirely disappeared; his vision was restored so that he could see minute objects on the ceiling as he lay in bed and his vertigo and ataxia had almost entirely disappeared. At no time during the convalescing period was the patient's condition such as to give any concern. He was kept under observation in the hospital for a period of two months, and inasmuch as there was not the slightest return of symptoms he was allowed to go home, with the understanding that he would return to the hospital if any of his cerebellar symptoms recurred.

Present Condition. He returned to the hospital for an examination March 5, 1906. About two years and four months had elapsed since the operation and his headache, nausea, and vomiting have never recurred. His vision is practically normal and he is now engaged as a laborer in the Pennsylvania Railroad shops at Altoona. It should be said, however, that he occasionally has some attacks of vertigo. His weight has increased to 184 pounds and he is in all other respects apparently perfectly well (Fig. 3).

FIG. 3—Showing the general robust appearance of patient one and one-half years after decompressive operation for tumor of the cerebellum.

CASE 5.—Tumor of the cerebrum; decompression operation affording relief from headache for a period of three years.

History. W. D., aged twenty-two years, was admitted to the University Hospital, Nov. 5, 1903, having previously been under the care of Dr. W. O. Hermance. He was admitted to the service of Dr. William G. Spiller, by whom the following history was elicited: He has been suffering from headaches since 1897 and for the past nine months they have been especially severe. He has furthermore often complained of nausea, vomiting, and dizziness and his sight is completely lost.

Examination. On examination there was found to be no involvement of either the fifth or seventh nerves. The movements of the tongue and of all the limbs were unimpaired. The biceps tendon and the triceps tendon reflexes were not specially active. The grasp of each hand was normal, as was the resistance to passive movements in all the extremities. There was no involvement of the bladder or rectum and no ataxia of upper or lower limbs. There was no deviation from normal as to stereognostic conception in either hand, the gait was normal, there was no tendency to sway or fall, there was no Babinski reflex on either side and the patellar reflexes were exaggerated. There was persistent ankle clonus on the right but none on the left side. There was no word deafness and no aphasia. His sister reported that about three months previously he was unable to speak at all for at least an hour, but that this was the only time he ever entirely lost the power of speech. He was at times delusional, and imagined he was being put into a hole. He had what he calls "sinking spells," in which he felt weak and his heart stopped beating.

About six months prior to his admission to the hospital he complained of stiffness (?), probably weakness, in the back, left side of the neck, in the left arm and left leg. He had never had any convulsions, but from April to August of the present year, his whole body would get stiff for about half an hour. His memory is better than it used to be. He listens attentively to what is read to him and remembers it better than the persons who read it. The headache had been frontal and bilateral until February of this year and it seemed to have become more localized to the left temporal region.

Dr. Thorington, who had examined his eyes, reported that there were no ocular palsies, but choked disk in both eyes, slightly more advanced in the left. There had been numerous hemorrhages, large and small, old and recent. Examination of the urine on one occasion prior to his admission to the hospital revealed a few hyalin casts and a small quantity of albumin. Since the examinations at the hospital, after repeated examinations, only on one occasion was a suspicion of hyaline casts, at no time was there albuminuria.

November 5, 1903, Dr. Shumway made the following ophthalmic report: No light perception. Right eye, atrophy following choked disk. Nerve head much swollen, veins tortuous, no hemorrhages. Left eye, nerve head still more swollen, some atrophy, hemorrhage on the nasal side of the nerve, numerous white points of exudation.

6th. It was noted on this date by Dr. Spiller that pupils were dilated, there was no reaction to light and no ocular palsies. The ophthalmic reflex was present on each side. Patient closed the eyelids firmly and wrinkled the forehead well on both sides, the tongue was protruded straight, not wasted and there were no fibrillary tremors. His hearing was apparently not affected. He swallowed without difficulty. There was some tenderness to percussion over the left temporal region. There was no word deafness nor motor aphasia.

Upper Limbs. Movements of the upper limbs were free at all points. The biceps and triceps reflexes hardly obtainable on either side. Grasp of each hand and resistance to passive movements were normal. Sensation for touch and pain normal in all parts of the body, and the sense of position and stereognostic conception were unimpaired. There was no wasting.

Lower Limbs. Voluntary power normal, no hemiasynergy on either side and no wasting of the lower limbs. The sense of position was normal on both feet. The patellar reflexes were distinctly exaggerated on either side and more prompt on the left side. There was a slight indication of ankle clonus on the right side, although clonus was not as persistent as at the last examination. There was no clonus on the left side. The Achilles tendon reflex was exaggerated on each side, but more so on the left. The patient stood well with his feet together and the eyes open or shut. His gait was normal, although it was uncertain on account of his blindness. There was no Babinski on either side.

Further examination of the other organs including those of the thorax and abdomen proved negative.

Operation. Craniectomy was performed by Dr. Frazier under ether anesthesia and an osteoplastic flap was reflected in the left frontal region. It was noted at the time that the skull and the dura were abnormally thick. There were no adhesions between the dura and the skull. Pulsation was visible and the brain did not bulge when the dura was reflected. Especially at the superior and anterior aspect of the opening the consistency of the brain seemed abnormally soft and an exploratory needle was introduced in various directions, but with negative results. The dural flap was replaced with sutures and the bony portion of the osteoplastic flap was removed for the purpose of relieving intracranial pressure.

Subsequent History. The patient remained under observation in the hospital until January 27, 1904, at which time it was noted that he had had no headaches since Dec. 28, 1903. His general condition had improved and he had gained in weight and strength. The last ophthalmic examination prior to his discharge from the hospital made Jan. 1, 1904, notes that the nerve is becoming more and more atrophied

April 15, 1904. The patient was admitted to the hospital again with a history of having had no recurrence of headache after he had been discharged; from this time on the headaches recurred generally on the right side of the head in the occipital region, accordingly was it

deemed advisable to perform a second palliative operation and on April 16, 1904, Dr. Frazier performed an osteoplastic operation, reflecting a flap from the right temporoparietal region, removing a flap 10 cm. broad and 7 cm. wide. It was noted at the time that there was no visible pulsation and that the brain appeared to be under considerable tension. The bone at the margin of the upper aspect of the opening appeared abnormally dark in color and unusually porous. An exploratory needle was introduced into the pons at about the middle of the opening but no fluid was detected.

Following the operation the patient complained for a few days of a severe supraorbital neuralgia which was attributed to the pressure which had been effected by the use of a pneumatic tube applied for the purpose of controlling hemorrhage. The patient was discharged from the hospital April 28th, about two weeks after the operation. His headaches had not entirely disappeared, although they were comparatively mild in character and the patient no longer required hypodermic administration of morphia to which he had been accustomed heretofore.

Present Condition, May 1906. The last observation was made two years and six months after the first operation and two years and one month after the second operation, and at this time it was reported that the patient had enjoyed almost absolute relief from his headaches. He is able to perform the duties connected with the management of a cigar store and with the exception of his loss of eyesight he appears to be entirely well. The optic neuritis was so far advanced when the patient was first seen that the possibility of saving his sight was out of the question.

Case 6.—Tumor of the cerebrum.

Patient. M. B., aged seventeen years was referred to the University Hospital, by Dr. R. Ross Jordan, Tyler, Clearfield County, Pa., and transferred from the service of Dr. Charles K. Mills, October 9, 1904.

History. He was struck on the back of the head nine months ago. He was not unconscious at the time he fell. About an hour later he became dazed, walking around aimlessly, remaining in this state for about half an hour. On Jan. 28, 1904, he was seized with shortness of breath, succeeded by tingling in the ears, and fell to the ground. It was said that during the convulsion his eyes were turned from side to side and that the whole body with the exception of the hands and wrists, fell into a state of spasm, lasting from five to seven minutes, with frothing from the mouth. Since that time he has had five attacks of this character, the later attacks having been preceded by violent occipital headache and vomiting.

Examination. He has marked optic nueritis, complains of intense headache and occasionally vomits. There is no hemiasynergia on either side. No paralysis of either facial nerve, the masseter, and temporal muscles contracting well on either side. Sensation for pain and touch is equal on both sides, so that there is no involvement of either the sensory or motor root of the fifth nerve. The extraocular movements are normal, but there is a lateral nystagmus when looking from either the right or left. The tongue is protruded straight, moves freely and there are no tremors. The head is not tender to percussion.

Upper Extremities. Grasp of each hand is equal and strong; sensation for pain and touch normal in each upper limb and it is the same on both sides. Stereognostic perception is normal in both hands. Biceps and triceps tendon jerk are not distinct in either side. There is no muscular atrophy. Resistance to passive movements is normal in both upper extremities. In the lower limbs no hemiasynergia. Resistance to passive movements normal, patellar reflex normal on each side, and there is no Babinski reflex. Sensation for touch and pain are the same on both sides, gait and station are normal with the eyes open or shut. There is not the slightest trace of hemiparesis or disturbance of sensation on the left side.

Ophthalmologic Report. From the service of Dr. de Schweinitz. Ophthalmic diagnosis hemianopsia. Pupils react normally to light and accommodation, the muscle balance normal; eye-grounds, media clear; O. D. marked optic neuritis, 5 D. no change in macula; O. S. swelling of disk 5 D; a few small fresh hemorrhages in the fundi. No change in the macula.

Operation. Dr. Frazier, Oct. 10, 1904. Inasmuch as the symptoms pointed entirely to a lesion in the occipital lobe, an osteoplastic flap was reflected exposing this region. The dura exposed in the opening presented a mottled appearance as though the seat of an organized traumatic or inflammatory exudate. There was slight visible pulsation and there seemed to be considerable tension. When the dural flap was reflected the brain immediately bulged through the opening even beyond the level of the scalp. From the opening a jet of yellowish-red fluid spurted three or four inches. About 45 c.c. of fluid were evacuated in this way. In order to close the defect it was necessary to reflect a flap from the pericranium inasmuch as the brain still bulged considerably through the opening. This was taken from the section of bone contained in the flap and the bone itself was removed. The wound was closed with interrupted silkworm-gut sutures and drain introduced through counter openings.

Subsequent History. October 13*th.* Since the operation the headache had entirely disappeared and the patient is now able to see objects which he could not before the operation.

24*th.* On the date of his discharge from the hospital it was reported that the patient felt better than he had for some months and that the vision of both right and left eyes had improved.

R. E. V. before the operation 6/30, at the present time 6/22.

L. E. V. before the operation 6/30, at the present time 6/15.

There is still a left hemianopsia and the swelling of the disks has decreased from 5 to 3 D.

Dec. 21, 1904. The patient was readmitted to the hospital. He returned to the hospital chiefly owing to the fact that the hernia cerebri had increased and especially for the past two weeks his vision had been failing. During the past two months he had gained forty pounds Examination of the eye-ground showed that the choked disk had entirely subsided, but that there was marked optic atrophy. There was left lateral hemianopsia for light only.

23*d.* The original field of operation was exposed and the dura was found intact. On reflecting the latter a canula was introduced and immediately a large quantity of blood-stained fluid escaped. Immediately after the evacuation of the fluid the hernial protrusion collapsed. The question arose at the time of the operation as to whether we were dealing with a cyst of the occipital lobe or the dilated horn of the lateral ventricle. No evidence could be detected of a neoplasm in the neighborhood of the operative field. The wound was closed in the usual way.

29*th.* Patient has made a satisfactory convalescence from the operation. There has been a free discharge of cerebrospinal fluid from the wound, requiring reinforcement of the dressing from time to time.

January 27, 1905. The patient was discharged from the hospital today, the wounds having healed *per primam* throughout. The hernia was not so prominent as it was before the operation. The patient's condition, with the exception of his impairment of vision, is entirely satisfactory. The optic atrophy which was discovered after the choked disk had subsided of course precludes the possibility of his recovering his vision. In a letter received from him, February, 1906, the patient reports that he is feeling very well, has had no bad spells, and is now in attendance at a school in Pittsburg, Pa.

Case 7.—Tumor of the left lateral lobe of the cerebellum. Decompressive operation, followed by striking improvement.

History. Inasmuch as this case was reported in full,[1] it will be necessary to refer here only to the salient points.

Patient. F. M., aged ten years, was referred to Dr. Frazier's service at the University Hospital by Dr. D. J. McCarthy, March 7, 1904. The essential symptoms in the case were a gradual increase in ataxia

[1] See Dr. Mills' paper "The Diagnosis of Tumors of the Cerebellum and Cerebellopontile Angle, especially with Reference to Their Surgical Removal," New York and Phila. Med. Jour., February 11 and 18, 1905, pp. 91–96.

and pronounced headache, vertigo, and vomiting. There was a marked degree of choked disk on both sides.

Operation. March 13, 1904. Dr. Frazier removed the bone overlying the left lobe of the cerebellum and proceeded to explore the hemisphere for a tumor. Exploration failed to reveal the presence of a tumor and before closing the dura, one-third of the cerebellar hemisphere was removed. The effects of the operation were most gratifying. At his discharge from the hospital on March 27th, his condition was noted as greatly improved. His whole disposition had changed; he was bright and cheerful and complained neither of headache nor vomiting.

Second Operation. November, 1904, the patient returned to the hospital because of the recurrence of some of his symptoms. On the following day the cerebellar fossa on the affected side was explored and an infiltrating tumor about the size of a walnut was found and removed.

The value of the palliative operation in those cases in which the tumor cannot be localized is well illustrated by this case. Between the date of the palliative operation and the time at which the tumor was finally found and removed the patient had been comparatively free from any subjective disturbance.

Case 8.—Suspected tumor of the cerebellum. Decompressive operation including removal of a portion of one cerebellar hemisphere, followed by considerable relief as to the vision, headache, vomiting, and vertigo. Death of the patient seven months later. No autopsy.

Patient. P. K., aged fifteen years, entered the neurological wards of the University Hospital in the service of Dr. William G. Spiller, May 9, 1905.

History. Eight months ago the patient complained of headache all over the head associated with vomiting. The attacks of vomiting were irregular, sometimes twice a day and again not oftener than twice a week; in the interval, however, he was occasionally nauseated. He complained for some time also of dizziness and difficulty in locomotion. He had never had any convulsions.

Examination. Dr. Spiller, May 12, 1905. Conjunctival reflex is distinctly impaired on the left side; corneal reflex normal, both cornea and conjunctiva are normal on right side. Movements of the face are normal on both sides and there is no involvement of motor or sensory root of the fifth nerve. Sensation for touch and pain is not impaired. Movements of the eyeballs in all directions are somewhat impaired, and somewhat inco-ordinate. Tongue is protruded straight, there is no atrophy and there are no fibrillary tremors. Hearing for the voice appears to be normal in each ear, speech and intelligence normal. When sitting up the patient holds his head fairly erect, possibly with a little tendency to incline it to the left.

The grasp of each hand is normal, finger-to-nose test normal on each side. Neither biceps tendon reflex, triceps tendon reflex, nor the wrist reflexes are distinct on either side. Sensation for both touch and pain normal in both upper extremities. There is no wasting in the upper extremities.

In the lower extremities the voluntary movements are normal, and there is good resistance to massive movements. The patellar reflex is very prompt, even exaggerated on the right side, but not quite so prompt on the left side. There is no ankle clonus. The Achilles jerk on the right side is prompt, but not so prompt on the left side. There is no Babinski reflex on either side, the smaller toes being drawn downward, the great toes remaining still. Sensation for touch and pain is normal in each lower extremity, the cremasteric reflex is exceedingly prompt on the right side and prompt, but not so markedly on the left. The musculature of the lower limbs is poorly developed, the patient has some difficulty in standing. On standing with his feet close together, even with his eyes open, he usually falls to the left and backward. His gait is very ataxic with a marked tendency to go backward, and to the left. Hemiasynergy is not present on either side.

Provisional diagnosis, cerebellar tumor, more likely on the left side because of the tendency to hold the head to the left, to fall to the left and backward and because of the impairment of the left conjunctival reflex, and of the less degree of exaggeration of tendon reflexes on the left side.

May 12th, 1905. Ophthalmic report by Dr. Shumway. Completely blind in the right eye, left vision about 1/100. Both pupils are widely dilated. The right pupil does not respond to light and the left responds sluggishly. There is some limitation of the movements of the eyes, particularly of inward movement, the left eye not approaching within 5 mm. of the inner angle; the movements are very jerky in character. There is a high-grade optic neuritis of the right eye which is going into secondary atrophy of the nerve. The veins are very tortuous and there is a small hemorrhage on the outer side of the nerve and an elevation of 6 D. In the left eye there is also an optic neuritis and of a milder degree with an elevation of about 4 D. The left nerve is also becoming atrophic. The patient was referred to the surgical wards.

Operation. May 17, 1905. Under ether anæsthesia, Dr. Frazier performed a decompressive operation. The exposure of the left cerebellar hemisphere was attended with unusually free hemorrhage particularly from those sinuses which have been described on previous occasions as existing in the occipital bone in the neighborhood of the occipital protuberance. When the dura was opened the cerebellar tissue bulged considerably but on the surface of the hemisphere and to a depth of about one inch, no pathologic condition could be demonstrated. About one-third of the hemisphere was removed and the cerebellopontile angle exposed but with negative results. A very good exposure of the seventh and eighth nerves was obtained, and they were demonstrated to the eight or nine physicians who were witnessing the operation. No further exploration was made and the wound was closed.

Subsequent History. The patient reacted from the effects of the operation. Dr. Shumway reports that the optic neuritis had subsided very much, the apex of the swelling in the right eye is now only 3 D. as compared with the 6 D. before the operation, and the left eye 2 D. as compared with 4 D. before the operation. The nerves are becoming somewhat atrophied. The patient's vision has improved particularly in the left eye, so that he can count figures at a distance of two feet.

July 19th. Reported to-day that the patient can walk around the ward without any assistance, although still somewhat unsteady, but, however, no tendency to fall in any particular direction. He has now no headache, and his vision has been so improved that he is able to distinguish faces and objects.

No opportunity was afforded to make any observations after the patient was discharged from the hospital, and in answer to a letter of inquiry written in January, 1906, we learned that the patient had died December 24, 1905.

Case 9.—Suspected tumor of the cerebellum in which a decompressive operation entirely relieved the subjective symptoms.

History. S. L., aged twenty years, patient of Dr. T. H. Weisenburg and Dr. M. Radcliffe, was admitted to the University Hospital, Oct. 25, 1905, with the following history:

Family History. Father died of pneumonia. Mother is living and well. Two sisters and six brothers all in good health. No history of nervous disorders, tuberculosis, renal disease, cardiac disease or neoplasm.

Social History. Patient was born in Austria and came to this country when three years of age. Engineer by occupation. Uses alcohol and tobacco in moderation. Patient has a small urethral discharge at the present time of one month's duration. There is no syphilis.

Previous Medical History. Patient had measles during infancy; otherwise he has always been in excellent health. He was well until one year ago, when he began to experience nausea, followed by vomiting, with pain of a severe character, starting in the nape of the neck and shooting upward to the top of the head. At first these attacks were rather frequent, occurring every day or every other day, but they have greatly decreased in frequency. Two months ago the sight in the

left eye began to fail and now he can distinguish only shadow and light. At about the same time he noticed that he was deaf in the left ear. On attempting to walk he feels giddy and staggers. This began about three or four months ago and has not increased much since then. Turning the head from side to side and backward causes some pain, but not severe. Lifting causes severe pain with blurring of vision. No motor paralysis.

Examination, by Dr. Weisenburg. Station with eyes open and shut good. Gait with eyes closed, good, though occasionally he has tendency to walk either to right or left.

Eyes. Pupils dilated with atropin. Convergence impossible with left eye, *i. e.*, on attempting to look at nose, the left internal rectus is weakened. Associated ocular movements to right and left are perhaps affected; *i. e.*, he can look either to right or left to the normal extent, but in a short time the eyeballs have a tendency to jerk back toward the median line. Upward and downward associated movements are normal. No diplopia. Ophthalmoscopic examination shows marked choked disk on both sides, especially the left. Both optic nerves are much swollen and hemorrhages are profuse. The appearance is that of an albuminuric retinitis.

The fifth, the seventh, and the twelfth nerves are normal. Hearing seems to be diminished on the left side. There is no trouble in eating; no dysphagia; no dysphonia. Memory is good. Both upper and lower limbs are normal in form. Reflexes and sensation are normal. There is no ataxia on either side. No involvement of bladder or rectum. No hemisynergy. Touching conjunctiva on either side does not elicit any movement of eyeball while corneal reflex is present. There is no Babinski. The results of the examination of the nose, throat, and larynx by Dr. Grayson and of the sense of hearing by Dr. Randall were entirely negative.

Operation, Oct. 26, 1905. A decompressive operation was performed by Dr. Frazier, which consisted in a suboccipital craniectomy, the bone overlying the left cerebellar hemisphere was removed. There appeared to be an increased amount of intracranial tension and the dura did not present its normal pale, bluish color, but in most places and particularly in the upper and inner angle, it was yellowish, opaque and dotted here and there with whitish-yellowish specks. The dura was not incised.

The operative recovery was entirely uncomplicated. The wound healed throughout *per primam*.

31st. Dr. de Schweinitz made an ophthalmic examination and reported a right choked disk, plus 10 to 11 D.; left choked disk, plus 9 D. and no fresh hemorrhages.

November 3d. Dr. de Schweinitz reports O. D. choked disk, plus 11 D., some fresh hemorrhages. Vision 6/22. O. S. choked disk, plus 9 to 10 D., but more contracted laterally; fresh hemorrhages.

December 22d. Dr. de Schweinitz reported as follows: O. D. 6/12 subsiding neuritis, plus 7 D. O. S., subsiding neuritis, plus 7 D. It will thus be seen that choked disks have subsided about 4 diopters since the operation.

December 23d. The patient was discharged from the hospital to-day. Since the operation his vision has improved considerably.

January 29, 1906. Patient reported at the hospital for examination and said that there had been no headache, nausea, or vomiting. O. D. the disk can be distinctly seen, slight swelling of the edges, only about plus 1 D. O. S. disk apparently normal. This is one of the most striking effects on choked disk after decompressive operations that we have observed and is particularly interesting in that the results were obtained without opening the dura.

May 29th. The patient now has some headache, but much less than he had before the operation. He is occasionally dizzy. The patellar reflexes are a little increased. Gait and station are good even with eyes closed. Dr. de Schweinitz reports: Subsiding optic neuritis. R. E., marked loss of capillarity, especially temporal half disk swollen, 5 D. (eyeground 3 D.), hence actual elevation 2 D.; vessels shrinking; some exudate in macula. L. E., well-marked subsiding neuritis and postpapillitic atrophy.

CASE 10.—Tumor of motor region.

History. P. S., aged twenty-five years, was referred to Dr. Spiller by Dr. de Schweinitz.

Family History. Father and mother living and well. No history of neoplasm, tuberculosis, liver or kidney disease. Cousin became insane and committed suicide. Mother says the whole family is very nervous.

Social History. Went to school until eighteen years of age, then studied law for three years, but was forced to give it up on account of his nervous condition, then became a fireman on a locomotive. Smokes to excess; drinks alcohol in moderation.

Note from Dr. de Schweinitz: "Double optic neuritis (choked disk), visual fields normal. No palsy of exterior muscles. Choked disk about 5 diopters."

Up to eight years of age had almost every infectious disease. When eleven years old he went to bed well one night and awoke blind and remained so for four months (treated at St. Agnes' Hospital). Sight gradually returned. According to his mother, "eyeballs were solid red, like clotted blood." Until seventeen years of age, he had fair sight and did not wear glasses. At seventeen, he began to be very nervous, and it was then that he began to take "weak spells." About once a month he would suddenly become weak, his knees would give way and he would fall to the ground, but would not lose consciousness. These fainting spells disappeared after a while and have not been present since he was eighteen years of age.

At twenty-one years of age he again wore glasses. His sight gradually diminished and he suffered severe pain in his eyes, especially behind the eyes. Temporary attacks of blindness, lasting a minute or a few seconds, occurred sometimes. He has always been a heavy smoker since he was seven or eight years old. He has averaged twenty to twenty-five cigarettes daily and also a pipe and a cigar a day. He had gonorrhea three years ago, but has not had a chancre or other venereal sore. He has been always subject to headaches, but within the past year, pain has been almost constant, worse at night, preventing sleep, and associated with attacks of vertigo, weakness, nausea, and vomiting. The headache is chiefly in the vertex, but sometimes occipital and above the eyes. He had a severe fall and struck on the back of his head when a child. Weakness disappears at will; if he "were to give in to it he would go in a heap." He has never had convulsions, but says that several times he has had attacks in which the whole left side, arm and leg, especially the leg, became numb, "as though dead;" the arm was only a little affected. He has no paralysis or paresis anywhere. He was a fireman on a locomotive three years and was so nervous that he gave up the work. Every little noise would make him jump, and he was always expecting something to happen, "lost his nerve," as he expressed it. Masturbated freely before sixteen years of age.

Examination. Sensation seems normal everywhere and to every form of stimulation, and there is no astereognosis and no loss of muscle sense. Ocular movements are good. Slight nystagmoid movement is seen on extreme lateral excursion, especially to the left. Reflexes are normal. There is no Babinski and no ankle clonus.

Cardiac condition: Irregular heart action without marked accentuation of either aortic or pulmonic sounds.

Patient states that the attacks of stiffness of left lower limb previously mentioned are usually preceded by much greater headache, a "sensation of something inside expanding and bursting out." They frequently occur at night and in them the left leg becomes very rigid and is drawn across the right, but it can be voluntarily moved. The left arm is to a less extent involved and still less the left face. During the attack, consciousness persists, but the whole left side feels as though "dead." He has almost constantly a blowing tinnitus aurium; only on the right side. He quit railroading in November, 1905, and since then has had only one or two attacks of spasm; previously had one or two weekly.

March 20, 1906. Yesterday morning, in getting out of bed he had headache. Between 10 and 12 o'clock he became weak in his knees,

but did not fall. In the afternoon he vomited and complained of intense headache and became unconscious. The left arm was flexed on the forearm and was stiff. The left lower limb was stiff and probably the left side of the face was affected. He was unconscious all night and very noisy and hard to restrain. This morning he is perfectly conscious, but in an agony of headache, crying out at times and tossing about in bed, clutching at any one near him and begging for relief. There is no motor weakness in any of the limbs, but he has some slight disturbance of sensation in the right hand. Stereognostic perception, the sense of position and tactile sensation are normal in each hand. The spasms which he has had have been in the left side and have always been tonic (never clonic). The patellar reflex is exaggerated on the left side and possibly slightly so on the right. Achilles tendon reflex is not exaggerated and there is no Babinski reflex.

Operation by Dr. Frazier. March 20, 1906. Under ether anæsthesia the usual motor opening was made, the flap measuring 3½ x 4 inches in width and length. When the osteoplastic flap was reflected it was noticed that at a point about 2½ inches from the front of the posterior margin of the opening and just below the superior opening the dura had already been punctured by the neoplasm, and immediately overlying this point the bone had been almost entirely worn away by the tumor. There was no visible nor palpable pulsation. The exposed dura was of a greenish hue and gave the appearance as though there were beneath it numerous large vascular channels. There was a peculiar soft fluctuating sensation communicated to the examining hand. An exploratory incision was made in the dura, beginning at the point where it had ruptured spontaneously. A tumor was immediately exposed, apparently of the infiltrating character and filled with large vessels. Its removal was considered impracticable. The dural incision was closed and the lower half of the bone contained in the flap as well as a considerable portion of the temporal bone were removed. The wound was closed as usual with interrupted silkworm-gut sutures and the drainage introduced through two counter openings.

21st. The headache, of which he complained so bitterly before the operation, has entirely disappeared. Patient can move his left leg, but has no movement in his left arm, forearm, or fingers. Sensation is not impaired. There is some impairment of the left facial nerve.

22d. The movements of the left lower limb are still unimpaired. The left upper limb is completely paralyzed, as is also the lower part of the left side of the face, the muscles supplied by the superior branch of the facial nerve being weak. The tongue deviates a little to the left when protruded. The left biceps and triceps reflexes are not distinct; the left patellar reflex is exaggerated. There is no ankle clonus on the left side.

Subsequent History. March 23d. Drainage removed to-day and wound in excellent condition.

25th. Dr. de Schweinitz reports that in the right eye there is optic neuritis, a greenish-white swelling confined to the disk and covered with numerous particles, probably cholesterin. There are no hemorrhages. Swelling of the disk is plus 3 D. In the left eye the conditions are precisely similar; swelling of disk, plus 4 D. Vision O. D. 4/25, O. S. 4/12.

26th. Patient's general condition is excellent. The dressing has been removed and he is up and about the ward.

27th. For the first time the patient can lift the left arm and raise his hand over his head without any difficulty; he can flex his fingers.

30th. Patient still has some weakness in the lower side of the face, the left upper arm is still weak, although power is gradually returning. Tactile sensation, sense of position, stereognostic conception are normal in the left hand. He is able to walk unaided.

April 1st. Dr. de Schweinitz reports, under date of to-day, optic neuritis in right eye plus 3 D., in left eye, plus 4 D. O. D. V. equals 4/20 (?), O. S. equals 4/10 (?). Vision is very much blurred. Evidence of temporary blindness.

April 4th. The patient was discharged from the hospital to-day, having had absolutely no recurrence of headache.

Case 11.—Tumor of cerebellum.

History. E. F., aged sixteen years, was referred to Dr. Spiller, July 16, 1904, by Dr. J. S. Baer and Dr. R. G. Curtin. The father of the patient possibly had had syphilis. The menses ceased about two years ago; having begun when she was fourteen years of age, they had, therefore, been present only a short time. For about one year she had had a severe sensation of pressure at the back of the head, as though someone were pressing her brain out, but this sensation is not felt now. She has had headache, not localized to any one part of the head, and has had "neuralgia" in the left side of the forehead about a year. Before December, 1903, the headache was severe. About a year ago she began to have nausea and vomiting, at first about every six weeks, but these symptoms gradually became more frequent until they occurred every two or three days. The vomiting had no relation to eating. About a year ago she began to be dizzy, but has not been dizzy since February, 1904. Dr. Risley has recently discovered optic atrophy, secondary to choked disks. She has never been unconscious. She has had difficulty in lying on her right side, but this sign seems to have disappeared. Lying on the right side caused her head "to kind of draw." She has never had convulsions. Sight has been failing about two years. Difficulty in walking was noticed about November 1903; she staggered, and the staggering seemed to be more to the left.

Present Condition, July 16, 1904. There is no involvement of either seventh nerve; masseter contracts well on each side, tongue protrudes straight, not atrophied and shows no fibrillary tremors. Movements of eyeballs are free in all directions, but distinct nystagmus is observed in turning the eyes far to the left or right, and probably is more intense in turning the eyes to the right. The right pupil may be a trifle larger than the left. The reaction of the pupil to light is preserved, also in convergence. Accommodation cannot be tested because of poor sight. She can count fingers with either eye, but the sight is more impaired in the left eye. She hears a low-ticking watch one or two feet from either ear, and has not noticed any deafness. She has had buzzing in both ears, especially in the left, but Dr. Baer states that she has had accumulations of wax in the ears. The face is somewhat puffy and expressionless. The exit points of both fifth nerves are sensitive, but the left supraorbital foramen is more sensitive than the right. She now holds her head straight, but says she formerly inclined her head to the left. Sensations of touch and pain are normal in each side of the face.

Upper Limbs. All the movements are free; the grasp of each hand is normal. The biceps and triceps reflexes are not distinct on either side. Sensations of touch and pain are normal in each upper limb. The finger-to-nose test with eyes closed does not show distinct ataxia.

Lower Limbs. Voluntary power is normal. The patellar reflex may be a little prompter than normal on each side. She staggers a little when standing erect with eyes closed, and the gait is uncertain, with a tendency to stagger more to the left. The gait is cerebellar in type, but the staggering is not intense. The Achilles jerk is not distinct on either side, nor is the Babinski reflex. Sensations of touch and pain are normal in the lower limbs.

Dr. W. H. Powell first examined the eyes in November, 1903, Vision of the right eye, 20/50; of the left eye, 20/50. Pupils react to light and accommodation. Peripheral vision normal; media clear, but fundus suggests a low grade of neuritis. In July, 1904, vision of the right eye was 20/100, of left eye 4/200, and she had optic atrophy and markedly contracted fields.

Chiefly because of the history of probable syphilis in the father, Dr. Spiller employed mercury and iodide, and by Aug. 16, 1904, her gait had become less ataxic. By May 5, 1905, headache had disappeared, but about once a month she still had a drawing sensation, as though the brain were being pulled out. Ataxia was slight. The patellar reflexes were about normal.

February 22, 1906. Dr. de Schweinitz found typical postpapillitic atrophy.

Operation. March 9, 1906. Suboccipital craniectomy was performed by Dr. Frazier under ether anæsthesia. The operation consisted in

removing that portion of the occipital bone overlying the left cerebellar hemisphere.

Subsequent History. March 28, 1906. Since the operation was performed the condition of the patient has improved, but only to a moderate degree. The pain referred to the arms has been very much less severe and at times she has had none at all. Her headaches also have been less severe and less frequent. Although confined to bed for the past year, she is now able to get up in a wheel chair. Although the dura was neither incised nor removed at the operation, there is quite marked bulging over the left cerebellar hemisphere, showing that the dura has yielded to the pressure from within and that it is possible for a hernia to develop without opening the dura.

Second Operation. April 4, 1906. After consultation with Dr. Spiller it was decided that, owing to the fact that the headache and pain in the arms had not been entirely relieved, it would be advisable and afford greater relief to the increased tension to split the dura. Following an injection of $\frac{1}{4}$ gr. of morphine, and under ether anæsthesia, the left cerebellar hemisphere was exposed by a muscle-splitting operation. A vertical incision was made through the middle of the original flap, the edges of the wound retracted and a crucial incision made in the dura about one and one-half inches in either direction. The cerebellar tissue bulged considerably through the opening, but the exposed tissue was normal in appearance. The musculo-aponeurotic layers of the wound were closed with catgut sutures and the scalp with interrupted silkworm-gut suture.

April 16th. The following notes were made by Dr. Spiller: The paralysis in the lower distribution of the right facial nerve supply is distinct, although the upper distribution of the nerve does not seem to be affected. She has slight weakness of the right upper and lower limbs. The patellar reflex is prompt on each side, but prompter on the right, and there is slight tendency to ankle clonus on the right side. The Babinski sign is present on the right side, but uncertain on the left side. There is no disturbance of sensation for touch or pain in any part of the body.

May 23d. For the first few weeks after the second operation the patient had occasional headaches and pain in the upper extremities. For the past two weeks, however, she has been almost entirely free from both these symptoms. She has gained in strength and is able to be up a considerable portion of the day. A hernia cerebelli has increased somewhat since the second operation (Fig. 4). She has recovered sufficiently from the effects of the operation and is sufficiently relieved to warrant her being discharged from the hospital. Her gait is still ataxic. She menstruated in May, 1906, the first time within a period of four years.

Case 12.—Cerebellopontile tumor. Decompressive operation, followed by disappearance of headache, vomiting, and by subsidence of choked disk.

History. E. D., aged twenty-four years, was referred to Dr. Frazier by Dr. Sherman Voorhees, of Elmira, N. Y. She was seen in consultation also by Dr. Spiller. About two years ago the patient noticed that her limbs were weak, that she would stagger in walking, although she did not feel dizzy. About one year ago she began to notice that her vision was failing. At this time she would have attacks, when for a few minutes everything before her would seem black; following the attacks she could see perfectly well again. At the same time she began to have attacks of nausea and vomiting, and noticed that she was becoming slightly deaf in her right ear. For the past three months she has had considerable headache, sometimes dull, at others, sharp and shooting in character. At the time of her admission, Feb. 16, 1905, she is practically blind and unable to walk.

Examination, February 17th. It was noticed that in showing her teeth, the right corner of the mouth is not drawn up nearly so well as the left, and in drawing up each corner separately, the movements on the right side are distinctly less than the left. On closing her eyelids forcibly the resistance to passive movements is less on the left side than on the right side; the masseter muscle seems to contract equally well on one side as on the other. The ocular movements are normal and there is no distinct nystagmus. There is no disturbance of pain and tactile sensation in the face, although she complains of a "queer" feeling on the right side of the face and right side of the mouth and of the face feeling numb, as though it were asleep. Further examination gives the impression that both the left temporal and masseter muscles contract a little more than the right, although it was subsequently found that on both sides the muscles respond equally well to Faradic current. The tongue is protruded straight and there are no fibrillary tremors. The right eyelid seems to be slightly more prominent than the left.

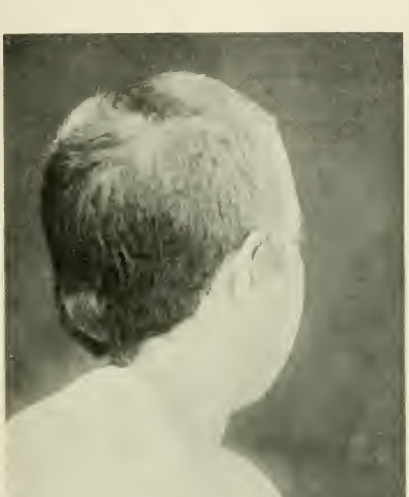

Fig. 4.—Showing a hernia cerebelli after a unilateral suboccipital craniectomy. The patient prior to the operation had been bedridden for over a year, is now able to be up and about and has been relieved almost entirely of her pressure symptoms.

In the upper extremities the grasp of each hand is normal. Biceps reflex is normal on each side; the triceps reflex and wrist reflexes are not distinct on either side; sensations for touch and pain are normal on both sides. There is slight ataxia on each side, a little more on the right.

In the lower extremities the patellar reflex is a little prompter than normal on both sides. There is no ankle clonus. The Babinski sign is uncertain on each side, as she resents any attempt to irritate the sole of the foot. The Achilles jerk is absent on both sides; there is no hemiasynergy and no weakness of any of the limbs; gait is slightly ataxic, specially noticeable when she turns; in walking the patient staggers more to the left than to the right. She staggers when her feet are together almost as much when her eyes are open as when they are closed.

Examination of Ear. Dr. Randall finds little hearing in the right ear by air or bone, except for the Galton whistle. Tests are slightly

contradictory, but indicate middle ear trouble on the right side, complicating semi-complete right acoustic paresis. Hearing on the left side is not impaired.

Ophthalmic Examination by Dr. Shumway. Pupils are dilated; right pupil responds when light is thrown in from the temporal side, in which position it is recognized. The left pupil does not respond to light and the eye is blind. There is choked disk on both sides; elevation on the right side is about 6 D. and on the left 7 D. The nerves are beginning to atrophy. The eye movements are carried out in a jerky manner, the muscles acting feebly, and the eyeballs return to primary position immediately. There is no paralysis of the ocular muscles.

Operation. February 23d. Under ether anæsthesia Dr. Frazier performed a suboccipital craniectomy, removing the bone overlying the right cerebellar hemisphere. Owing to the fact that bleeding was so profuse, it was decided to discontinue the operation at this stage until the patient had fully recovered from its effects.

A radical operation was performed two months later and was followed by death within five days (Figs. 5 and 6). After the decompressive operation the choked disk subsided from 7 D. to 3 D., although unfortunately, the optic atrophy was so advanced that it precluded the possibility of restoring the vision. The hearing improved somewhat after the operation and the nausea and vomiting ceased. Headaches disappeared almost entirely and the patient was able to get up and walk about the ward with but little assistance.

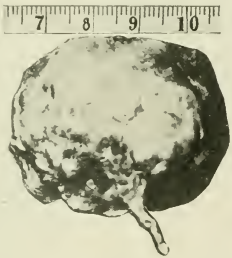

Fig. 5.—Photograph of fibroma removed at operation from the cerebellopontile angle.

Case 13.—Inoperable tumor of brain. Decompressive operation, followed by little or no amelioration of the symptoms, although prolonging the patient's life.

Patient. R. C., aged thirty years, was referred to Dr. Charles H. Frazier by Drs. Thomas O. Nock and Wharton Sinkler, March 15, 1906, the latter having seen the case in consultation.

History. There was a history of the patient having had an attack of vertigo while walking about three months ago, and had she not been caught by her husband, she would have fallen to the ground. At the same time she had some numbness in the left upper and lower limbs. Since that time she has had two attacks of numbness of the limbs, but no vertigo. She has had more or less persistent headache for the past year, occurring about three or four times a week, usually in the mornings. There have been no convulsions. Three weeks ago the symptoms became much more severe, headache more intense and numbness in the left extremities more marked. At this time it was noticed that the muscles of the left side of the face were gradually becoming weak, the muscles becoming paralyzed within a period of from four to five days. Up to this time there was no weakness in the extremities, but about a week after the involvement of the facial muscles was noticed the grasp of the left hand became weak, and about the same time weakness was noticed in the left lower limb. The upper extremity sometimes is flaccid, at other times spastic, but the lower extremity has never been spastic. The pulse has varied between 44 and 60. The respirations have been alternately shallow and moderately full, the respiratory rate ranging from 16 to 30 a minute. For the past four or five days her temperature has been subnormal. About eight days ago, for the first time, the patient became stuporous for variable periods of time. These periods of stupor have gradually increased, and during the past two days the patient has been almost comatose. This condition of mental hebetude was first noticed about two weeks ago.

Examination, March 15, 1906, by Drs. Nock, Sinkler, Frazier and Spiller. Stupor is so great that the patient can be roused but slightly. She lies in bed with her head turned to the right, but there is no deviation of the eyeballs. There is no tenderness on percussion of the scalp. She is able to move the eyeballs well to the right, although there may be slight impairment of the left eyeball to the right, but probably not of the right eyeball to the left. The right pupil is larger than the left. Neither pupil reacts to light. It is impossible to tell whether there is any deviation of the tongue or to test the muscles of mastication.

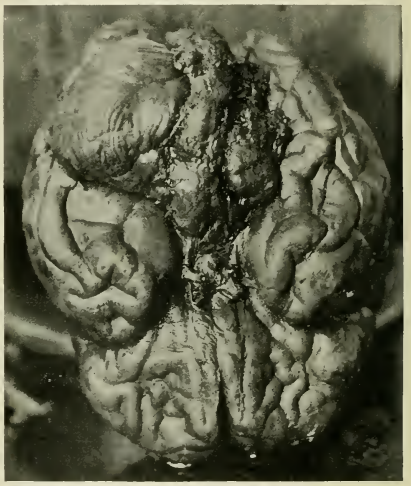

Fig. 6.—Photograph of brain showing portion of tumor remaining in the cerebellopontile angle after operation.

Left Upper Extremity. The left extremity is very weak, although she has a little voluntary power in it and can flex the limb feebly at the elbow. She cannot make a fist with the left hand. The biceps tendon and triceps tendon reflexes are present, but weak. Sensation is not disturbed.

Left Lower Extremity. The lower extremity is very weak, although she can move it slightly. The patellar reflex is present on the left side, but not very prompt. The Achilles tendon reflex is present on each side and about normal. There is no ankle clonus and the Babinski sign is very typical on the left side, as it is on the right, although not so pronounced. Pin-prick is perceived in the left lower limb.

Examination of the Blood. Systolic pressure, 165; hæmoglobin 65 per cent.; white blood corpuscles, 21,240.

Urinalysis. There is slight albuminuria, no sugar and a few granular casts.

Ophthalmic Record by Dr. de Schweinitz. This examination was made a week or more before the patient came to the hospital and disclosed a moderate optic neuritis of each eye, most marked on the right side. There are a few hemorrhages in the neighborhood of the optic disk. The neuritis appears to be in an early stage of its development; on the left side it is just beginning. The pupil reacts normally. There appears to be a divergent strabismus, usually more marked on the right side and probably dependent on paresis of the right internal rectus. Some examinations appear to indicate that there was failure in the movement of the eyeball upward, therefore some involvement of the right superior rectus. This was not certainly determined, as there did not appear to be much difference between the two sides; both lids droop to about an equal extent, but the droop is one probably due to weakness and not to paresis. The visual field, roughly taken by the hand, appeared to be undivided; at least there was no hemianopsia.

Operation. March 15, 1906. The date the patient was admitted to the hospital an osteoplastic operation was performed, in which the motor region was exposed. It was noticed when the flap was reflected that there was some bulging of the dura at the lower and posterior angle of the opening. An exploratory incision about one and one-half inches long was made at this point, at which the dura seemed very much thinner, as though undergoing atrophy from pressure. The brain contents bulged through the opening thus made, and an exploratory cannula was introduced for about one and one-half inches, as there was some reason for suspecting the presence of an abscess. It seemed as though the cannula entered a cavity; at first some brownish fluid flowed from the cannula and afterward pure blood. The exploratory incision was made about one-half inch behind the anterior margin of the opening and a small section of tissue removed for examination. Concluding the lesion was a subcortical one; we decided to discontinue any further exploration. A considerable portion of the bone in the flap was removed and the dural incisions and the incisions in the scalp closed.

From the date of the operation until the time the patient left the hospital, ten days later, the patient manifested but little, if any, improvement as a result of the operation. There were times when she seemed to be a good deal brighter than she had been in the immediate past, and also times when she had a little more movement in the left upper extremity. Mental condition, on the whole, was better, but apart from this there was very little, if any, change. It might be noted that the leukocytosis, which existed before the operation, continued afterward, and at one time the white blood corpuscles numbered 36,000. In a differential count that was made March 25, 1906, there were 94 per cent. of polymorphonuclear cells. The persistent leukocytosis in the absence of any wound infection was strongly suggestive of the presence of an abscess.

Postoperative History. May 24, 1906. A letter recently received from the patient's physician, Dr. Nock, says that her present condition is about the same. There is complete paralysis in the left upper and lower extremities and now gradual weakening of the muscular power in the right arm and leg. When awake the patient talks intelligently and is interested in what is going on, although there is a tendency toward confusion of ideas at times. Her appetite is good and she takes enough food to maintain her nutrition. Her temperature varies from 99 to 99.3. Pulse is regular.

We include the following case, which was in the service of Dr. Mills and Dr. Martin and was studied also by us:

Case 14. Stafford, male, aged forty-six years, was under the care of Dr. C. K. Mills in the University Hospital, in 1902. He was seen also by Dr. Potts and Dr. Spiller.

Fig. 7.—Tumor of the cerebellopontile angle.

The patellar reflexes and Achilles tendon reflexes were lost; the gait was ataxic. Headache, dizziness, optic neuritis, nystagmus and paræsthesia of the left side of the face were present among other symptoms. The diagnosis of cerebellar tumor was made. A palliative operation over the cerebellum was performed by Dr. Edward Martin in 1902. The patient's condition was much improved. He died in 1906 and a tumor was found in the left cerebellopontile angle (Fig. 7).

A REPORT OF THREE CASES OF PREMATURE SEPARATION OF THE PLACENTA FROM ITS NORMAL POSITION.

By William R. Nicholson, M.D.,
Assistant Obstetrician to the University Hospital.

Case I.—Mrs. S. began to bleed moderately during the latter part of her second stage. There were no symptoms of constitutional effect. The forceps were applied and a dead child extracted. It was evident that the death of the fetus had but just occurred. The placenta was easily removed and there was no subsequent bleeding.

Case II.—Mrs. M. had six children at term and one miscarriage. Married for fifteen years and is thirty-two years of age. After the miscarriage in 1901 (fourth month) she had temperature and chills and was curetted. In the early part of 1902 I performed a ventrosuspension upon her at the Gynecean Hospital. She was delivered in January, 1903. In this pregnancy she suffered a good deal of pain in the lumbosacral region and on examination at about the sixth month a mass was detected behind the uterus which seemed to be retroperitoneal, as determined by a sound in the rectum. Her labor was uneventful except that she suffered for several days from pains which had no dilating power, and which finally necessitated the introduction of bougies in order to start real labor. After this delivery she was well until August, 1904, when she "missed her sickness." I saw her first about the ninth of October and she gave the history of having had a marked uterine bleeding eleven days previously while asleep in bed. There had been no pain or at most but very little. Examination at this time showed that the uterus was enlarged to the size corresponding to that of pregnancy of two and one-half months' duration. I diagnosed a probable threatened abortion and advised appropriate treatment for that condition. Fifteen days later she reported that there had been bleeding at intervals since her previous visit and that the night before she had had a gush of blood while quiet in bed. There was pain felt in the left lower abdomen, of a dull character and almost constant. She thinks that the hemorrhages weaken her considerably. Pelvic examination on this date showed that the uterus was larger than normal for a three months' pregnancy, and that there were no signs of inflammatory disease in the area of the appendages. The uterine enlargement was general, although the anteroposterior was less than the transverse diameter. The condition of the cervix was noted as not being markedly softened. Two days later, on October 25th, she had another hemorrhage, also occurring in the night and more profuse than any preceding one. During this last bleeding there were marked expulsive pains. At this time her pulse was eighty. As there was no dilatation of the cervix and as the patient was sure that nothing "had come away," I advised opium by suppository. The next day, October 27th, there was again the report of a hemorrhage during the night, of about the same quantity as the last but with decidedly lessened amount of pain. Her pulse was not increased in frequency but was very weak. The vaginal examination showed that there was still an absence of cervical dilatation, while the uterus had apparently markedly increased in size, reaching at present to within a distance of three fingers' breadth of the navel. This increase, to the size of almost that normal for the fifth month of gestation, had taken place within a period of a very few days. Upon pressure the womb was not painful except at the left cornua, and very slightly so at that point. The patient stated that when bleeding occurred it was in gushes of fluid blood. There was now marked nausea and vomiting. The temperature was normal.

Upon the next day, the 28th, she gave the history of having experienced no bleeding or pain during the night. Upon examination, however, it was apparent that the uterus had increased in size since the day before, the distance of the fundus below the navel now being less than three fingers' breadth. As she rested on her back there was a distinct visible tumor between the navel and the symphysis, suggesting a fibroid in appearance.

The cervix was not so soft as the length of the pregnancy, judged from the size of the uterus, would warrant, while the uterine substance was softer and had a different consistence from the normally impregnated organ of the like size. Upon October 30th, she was admitted to hospital. There had been no bleeding since the 27th inst.

November 4th. No recurrence of bleeding; no dilatation of cervix; but slight increase in size of the uterus since last note, the fundus now being about two fingers' breadth below the navel. It does not seem as large transversely as its height would indicate that it should be. Very indistinct ballottement felt upon the right side of the uterus. As there had been no bleeding while at rest in the hospital she was allowed to go home. At this time I felt that the condition was probably one of cystic degeneration of the chorion villi, as the symptoms of bleeding and rapid increase in uterine size were both marked.

11th. Since the last note patient has been at home and reports that last night there was a profuse bleeding and that she has been bleeding somewhat for several days. Abdom-

inal examination showed the fundus slightly above the navel. Pulse 76. No clots have been passed.

13*th*. Readmitted to the hospital. The uterus to-day is not quite as large as upon the last mentioned date, being now about one finger below the navel.

17*th*. There has been quite a little bleeding during the last few days, and last night the nurse noticed that the uterus had decidedly enlarged and that later in the night there was a decided increase in the flow of blood with a corresponding decrease in the size of the uterus. Upon my examination to-day I found that the fundus was two fingers' breadth above the navel. Pulse a little over 100 and the patient says that she now feels badly. Upon consultation at this time with Dr. R. C. Norris it was decided that it would not be wise to wait any longer, and so the cervix was dilated a little by the branched dilator (to one and one-quarter inches) without ether, and the uterine cavity packed with gauze after the ovum had been broken up by placental forceps. Later in the evening as there was still bleeding, and as the temperature had become markedly febrile, ether was given and the cervix was slightly further dilated by the Bossi instrument and then continued by the fingers. Two small fœtuses, together with a mass of placental tissue, and liquid blood were removed. The uterus promptly contracted. Each fœtus was about four and a half inches in length. The fingers and toes were separated. Convalescence normal.

Case III.—Patient seen with Dr. C. M. Burk, aged about thirty-eight years, has had six children born at term and one miscarriage. All previous labors have been easy. As nearly as could be ascertained the patient was about seven months pregnant. The first symptom of trouble was a hemorrhage, reported as having been of large amount and which occurred several hours before I saw her. There was no pain felt at any time during the initial bleeding and no history could be secured pointing to any traumatism of pain preceding its occurrence. Upon examination there was found to be a slight flow of blood from the vagina, the cervix would admit the index finger with ease, and there had been no obliteration of the cervical canal. The membranes had already ruptured. The pulse was rather rapid, the general color was good, there was no pain, respiratory difficulty or restlessness. The size of the uterus and the apparent development of the child's head corresponded at least to the end of the eighth month of pregnancy. It is to be noted that upon vaginal examination there was a marked downward bulging of the anterior vaginal wall with an appreciably increased tension and a distinct feeling of doughyness. This was thought to be due to the presence of a placenta previa, but was in reality undoubtedly due to a collection of blood in the uterus, prevented from escaping by the head of the child, pressed down upon the unobliterated cervix. As the bleeding which, at first had been of an alarming nature, had, after the rupture of the membranes, become decidedly less in amount, and because of the above mentioned bogginess and bulging of the vaginal vault, the case was diagnosed as one of placenta prævia and a tampon having been placed in the cervix and vagina she was transferred to the Maternity Hospital. Upon her admission she declined any assistance and walked up stairs with perfect ease, and with no shortness of breath or cyanosis as a result. When seen and examined under good auspices soon after her admission, an immediate diagnosis of the condition as one of premature placental separation was possible, as no placenta could be felt in the lower uterine segment. As the cervix was rigid and as dilatation had not progressed during her trip to the hospital, the manual dilatation of the cervix was attempted and bags were also used. At this time the blood loss was slight and the general condition not that to cause any alarm, so it was felt best not to attempt to deliver by any forcible dilatation of the cervix. Within an hour her pulse showed signs of failure its rate having reached about 150. Sweating about the head and restlessness also developed. Ether was administered and as dilatation was found adequate and as the head was not engaged (L. O. P.) a podalic version was attempted. The child was dead as determined by palpation of the cord. After grasping the foot without much difficulty, it was found that rotation of the body was impossible for some reason, which I was at the time unable to explain. Forceps were therefore applied and extraction attempted but the head could not be engaged. The condition of the woman which at first, even after the pulse had so markedly increased, had not impressed me as being really dangerous, had now under the administration of ether and the continued blood loss, become alarming, so a craniotomy was done at once, when, to my chagrin, I found that it was impossible to deliver the crushed head because of some obstruction in the body of the child. The bones of the head were pulled out by the cranioclast but the trunk could not be brought into the pelvis. The head was therefore pushed up and after great difficulty the fœtus was turned sufficiently to allow an examination of the fetal abdomen. This was found to be greatly distended by a fluid accumulation and was at once partially evacuated (about a pint of fluid escaped) by a perforation of the groin. Extraction was with difficulty accomplished, until the abdomen had been born, when the remainder of the child followed at once. Upon examination of the infant it was found to be grossly deformed, one of its legs being much larger than normal for a full-term child, the toes of this foot being webbed, while the abdomen was greatly increased in size, from some cystic malformation even after the mutilating operation.

The condition of the mother improved after delivery and normal saline was administered with other free stimulation but shortly after the manual removal of the placenta which

was slightly adherent at one portion she suddenly died. The uterus had contracted perfectly and at once. Death was apparently due to shock.

Unfortunately no examination of either mother or fœtus could be obtained.

Premature detachment of the normally situated placenta may be defined as a separation of this organ, wholly or in part, and before the birth of the fœtus from its usual place of attachment above the contraction ring of Barbour or the retraction ring of Schroeder. The condition while rare is not an obstetrical curiosity, and therefore, as its occurrence jeopardizes both the mother and the child, it were well to have clear ideas as to the diagnosis and treatment of this accident, than which none demands more intelligent and prompt action on the part of the attendant. As to the actual frequency, it may be stated that it probably occurs once in about two hundred cases of labor when viewed from the basis of pathology alone, while considered from the side of clinical importance, its frequency may be placed as once in about five hundred cases.

Hippocrates held that all antenatal bleedings were due to a premature detachment of the placenta from the fundus uteri, where he believed that it was invariably attached. Until the year 1664 this idea was prevalent, Paul Portal at that date demonstrating the occurrence of placenta prævia, while in 1709 Schacker, in a postmortem examination upon a woman dying of antepartum hemorrhage, found the placenta adherent at the os uteri, and Hunter discovered the existence of the deciduæ reflexæ in 1770. In the latter part of the eighteenth century the unfortunate classification of "accidental" and "unavoidable" bleeding was first used by Rigby, in a thesis upon hemorrhage preceding the birth of the full-term infant. He does not seem, however, to have really distinguished between prævia and premature detachment, Holmes holding that his so-called cases of accidental hemorrhage are nothing more than instances of lateral placenta prævia.

Apparently the idea of placenta prævia became the fashion after its possible occurrence had once been firmly established in the minds of the profession; thus we find that when Baudelocque the younger published his essay, and gave the name of concealed accidental hemorrhage to one variety of antepartum bleeding, that he was met with an almost universal denial by his colleagues. Thus Boivin and Lachapelle denied the possibility of the condition, stating their objection, as based upon an experience of 42,000 labors, in the following words: "I (Boivin) cannot believe that the uterus, filled with the product of conception, can at any stage of the gestation admit so considerable a volume of blood, unless it has recently been emptied, nor can the quantity be sufficient to occasion the death of the woman."

This was the condition of the subject when Goodell published his classic paper. It is unfortunate, as pointed out by Holmes, that this author should have chosen as his title the term used by Baudelocque, namely "concealed accidental hemorrhage," since 27 per cent. of his cases showed some external bleeding. His paper was a most masterful exposition, his introduction showing by quotations from the standard works of the day, the paucity of knowledge of the subject possessed by teachers of obstetrics. With the exception of the ideas advanced as to the etiology of the condition, which the pathology of the present day has somewhat modified, with the exception of his methods of treatment which, we believe, offer a less favorable chance for maternal life than present day science may afford; and finally, with the reservation, that true cases of concealed hemorrhage are not more grave than certain ones of the mixed type, this paper, which has shaped medical thought ever since it was written, stands to-day as sound as when he published it.

In the consideration of the etiology there seems but little doubt that all cases when traced to their source are dependent upon a lesion existing in the deciduæ. In other words it is probable that excepting the instances of actually fatal traumatism to the mother, a basic pathological lesion of the endometrium is demanded, to supply the locum minores resistantiæ in the recorded instances of separation which have been ascribed to various minor accidents; accidents to which all pregnant women are frequently subjected, without, in the vast majority of instances, any ill-effects.

It is not necessary to go into the subject of endometritis decidualis; it is sufficient to call attention to the fact, now well known but unthought of when the paper of Goodell was published, that inflammatory processes in the endometrium which ante-date pregnancy may be the cause of trouble during gestation and after labor. One point, however, in the etiology is worth further investigation, namely, the part played by nephritis and possibly the kidney of pregnancy in the causation of low grade inflammatory processes in the endometrium with resultant extravasation of blood. Thus Lehman quotes Rosseau-Dumarcet's finding of eleven cases of albuminuria, in thirteen instances of premature detachment of the placenta; Lohlein, Winter, Veit, and Ruge, also report cases associated with chronic nephritis and attach etiological importance to the association; Fehling in a series of eighteen cases which had showed albuminuria, found twelve which gave inflammatory or hemorrhagic changes in the placenta. Meyer, who reports four cases of premature detachment of the placenta, did not find albumin in the urine, but in two of the placentæ he was able to demonstrate a condition of endometritis decidualis. von Weiss, in a series of seven cases of premature detachment, was able to demonstrate that in five cases with marked lesions of the kidneys, as proven in three by postmortem examination, and in the other two by a careful study of the urine, that there weer

marked exudative changes in the endometrium together with degenerations in the same region. In other words the presence of an endometritis decidualis was demonstrated in the cases, with a participation also of the superficial layers of the uterine muscle. The same author calls attention to the fact that while a round celled infiltration of the decidua is normal in early pregnancy, on the other hand in late pregnancy, it is always a sign of inflammatory change, and that while marked degenerative changes are normal to the decidua in the latter months of pregnancy, the degree attained in the above mentioned cases must be considered as pathological. It is well to bear in mind that placentary changes alone can not be considered as bearing a very important relation to the causation of premature placental separation, though it has been so explained by some observers, but that in all probability, as stated by Kaltenbach and Veit, there must also be a condition of serotinal inflammation or degeneration. In brief then it may be stated that the condition under discussion is not caused by the ordinary trauma, by shortened umbilical cord, by emotion, coitus, a false step, etc.; but that while, for the sake of completeness, some of these accidents may be admitted to a very secondary causal relationship, that the real condition, at the bottom of the occurrence are the changes occurring in the decidual layers of the ovum.

The practical value of this study rests upon the question of the possibility of making a diagnosis of premature placental separation at a time when treatment may be instituted with good hope of success. This is often a matter of great difficulty. Dr. Goodell in his paper makes a very insignificant statement, which it were well to bear in mind, namely, that "A concealed accidental hemorrhage stands alone in one respect, among many insidious diseases, in that its most prominent symptoms are common to other diseases, and mislead, while those peculiar to it can be elicited only after a very careful examination." While this is most markedly true in the cases of absolute concealment yet it also holds good in a proportion of those of a mixed type, which are so likely to be mistaken for placenta prævia, a mistake which can easily be a fatal error. Goodell places as the most important symptom the collapse, with its surface coldness, pallor, feebleness of pulse, dyspnœa, restlessness, retching, etc.; but while this is without doubt the most alarming symptom, it should not be depended upon for diagnosis as when developed it means that in the most instances the case is beyond hope. Pain, of a varying degree from a feeling of slight discomfort to a condition characterized as agony, is next in Goodell's list and it is to be remembered that this is most likely to be a prominent symptom in cases of complete retention of the extruded blood within the uterus. In the large majority of his series this pain was of a bursting character, was continuous, and was referred to by various observers as being "severe pain about the fundus uteri with a feeling of great distention as though she would burst," or as "a violent pain in the abdomen," or "suffering the greatest torture as though the abdomen would burst," or as "intolerable anguish." Among other symptoms may be mentioned the absence or extreme feebleness of the pains of labor; a marked distention of the uterus; a show of blood (in the concealed type this is often not evident until too late to be of diagnostic value); the presence of an accessory tumor (not at all constant); a tenseness of the presenting membranes (not constant); a serous discharge from the vagina, usually looked upon by the attendants as a discharge of liquor amnii, but which is, in reality, expressed blood serum from the intrauterine clots. Goodell thought that there should be a greater frequency of the sign last mentioned than has been noted by observers, since serum will pass an obstruction impassable to the blood itself. It is to be especially noted that the condition may, as stated by Goodell, be ushered in with the symptoms of a flatulent colic. This last was the symptomatology presented by his own fatal case when first seen by him.

The diagnosis then depends upon a group of symptoms none of which are diagnostic alone, nor of a nature to cause great alarm upon the part of the attendant when seen in their incipiency. Indeed a case may, as in an unreported instance known to the writer, show but one symptom, that of pain, until it has progressed to a degree precluding successful treatment. It is therefore of the most vital importance that the practitioner should be in possession of very clear ideas upon the subject, in order that the occurrence of these somewhat vague symptoms may attract his attention and that he have a definite plan of treatment which he may put in operation as soon as there be an indication for interference.

It appears to me from my own experience and from a study of the literature that there are two symptoms which, while neither are diagnostic and both may occur in other conditions, should nevertheless be considered as suspicious whenever met with. These are pain, of the character described above, and bleeding from the genitalia, encountered at any time during pregnancy. In other words, it is wrong to attach great importance to shock as a means of diagnosis since if it is allowed to become well marked before the diagnosis is made it will, in most cases be but a matter of scientific interest to make it at all. If the possible import of the two above mentioned signs be remembered, the practitioner will be in a postion to watch carefully for the further development of the symptom complex of the condition and to institute treatment as soon as a sufficiently sure diagnosis can be made. Another important sign is the peculiar, and rapid enlargement of the uterus, well shown in the second case reported by me, associated with a marked tenseness of the wall. To my mind the most important symptom in the cases of com-

plete concealment is pain, and any woman who presents an aberrant form of pain during her pregnancy, particularly if near term, should be looked at with suspicion. These cases of complete concealment are the most difficult of diagnosis; indeed the diagnosis in the early stages can be but provisional. Those cases associated with more or less frank bleeding or even only the discharge of serum present less difficulty. Here the main source of error is that they will be considered as cases of placenta prævia or threatened abortion. In them the vaginal examination will go far toward clearing up the diagnosis, as the finger can be inserted within the cervical canal as a rule, thus doing away with the question of placenta prævia, while the absence of the characteristic pains of labor ought, even if the peculiar form of pain noted above be present to prevent a mistake with regard to the latter condition. I cannot see that the differential diagnosis between premature detachment and rupture of the uterus is one to offer any great difficulty.

Even at the present day there is a marked lack of definite knowledge in the mind of the general profession with respect to the treatment suitable to this emergency. This may well be due to the fact that although, as a pathological entity, the condition is not an unusual one, that nevertheless cases of a marked severity are decidedly out of the common, and so, the needful individual experience being absent, deductions based upon personal knowledge cannot be expected. In addition there is still a good deal of haziness in the mind of the general practitioner as to the possibility of the occurrence of premature separation of the placenta, the majority of all cases presenting the symptom of antepartum bleeding being diagnosed as instances of placenta prævia, while the rare types of separation, without external bleeding, are not, unless the cause is revealed by a postmortem, correctly diagnosed in the great majority of instances. In the consideration of the treatment of these cases there are two minor measures which it will save time to consider at once in order to save repetition, namely, the reasons for and against the rupture of the membranes and the applicability of the vaginal tampon in the treatment of this condition. Both of these methods demand the respect due to age, since they figure in the treatment of all the early cases, along with the administration of ergot, but they do not deserve consideration otherwise. The membranes, it is to be insisted upon, are to be preserved in all cases until the cervix is so dilated that there is no doubt but that delivery can be readily effected after their rupture. Formerly, there was a distinct school that advised their rupture at the earliest possible moment, in order to cause contractions of the uterine muscle, with the aim of inducing hemostasis, dilatation of the cervix, and so a more rapid termination of the birth. Many reports are given which appear to show this to be a proper manner of treatment but upon careful study it is apparent that the successful result took place in spite of, and not because of, this interference. If labor be in progress, rupture of the membranes may be strongly indicated, but in the absence of true contractions it is evidently futile to depend upon excitation due to the escape of the liquor amnii, since, while awaiting the advent of the pains, there is ample time as a rule for the woman to die a half-dozen times. Last and least it is to be remembered that the intrauterine pressure, if preserved, may act, as a possible means of reducing bleeding from the wall of the organ. As an offset to this last statement it is never to be forgotten that the uterus does not constitute a plenum, the old idea which filled the obstetrical world with discord in times gone by, and so it is to be remembered that with intact membranes there may be a fatal concealed bleeding. It is thus seen that nature is often helpless in the presence of this emergency, and that a fatal outcome may result unless correct surgical principles are put into action and the bleeding vessels directly checked. It is hardly needful to say that the tampon has no place in the therapeusis of this form of bleeding since it can exercise no direct influence upon the bleeding vessels, while as an exciter of cervical dilatation it is last in the list of adjuvants.

It is clearly to be realized that the actual treatment of a marked case of premature placental separation is simply the emptying of the uterus as quickly as may be consonant with the safety of the woman, and of the woman alone; the child need not be considered. I would not be understood as implying that all or even the majority of cases demand this radical line of interference, the series of sixteen cases reported by Luig with no maternal mortality is alone a sufficient answer to any such idea, since all of them were treated in a very conservative fashion. These were however, but mild instances of the condition, with but little hemorrhage either internal or external, and were comparable to the first case reported by me. The marked examples of the condition which as I have said are fortunately rare, demand a different plan of action associated as they are with dangerous hemorrhage.

With reference to treatment, I would divide the severe cases occurring late in pregnancy or at term into two groups, viz., those in which, in the presence of considerable bleeding, the cervix is found to be either dilated by the presence of actual labor[1] or in the absence of labor easy of dilatation, and second those cases which, with considerable bleeding, offer an unobliterated and rigid cervix the dilatation of which would consume much time.

[1] It may be well to again call the attention to the fact that care must be taken to distinguish between the presence of true pains of a dilating value and those due to the distention of the uterus by the collection of blood within its cavity. The latter are continuous, of a tearing or bursting character and have absolutely no value as dilators of the cervix, since they are not in any sense associated with muscular contractions.

For the first of these groups the indication is to complete the dilatation by the use of the rubber bag, the dilator of Bossi, or by manual dilatation, according as the preference of the attendant, and the various degrees of necessity may indicate, the actual delivery of the child being secured by forceps, version or craniotomy. It is a good rule to perform craniotomy in such cases upon relatively slight indications, as the life of the child is practically always destroyed in the type of case under discussion. Unfortunately, however, the above methods will not suffice to meet the demands of those cases which fall within the second group, namely, those associated with a rigid unobliterated cervix. In such cases in the presence of grave symptoms there is no time for a slow dilatation by art or nature, for if the amount of blood appearing externally is not alarming, there is still no way to determine how much has been poured out within the uterus, nor, moreover, how soon the external bleeding may assume proportions which will immediately threaten life. In these latter cases no one can feel secure until dilatation has been secured, since until then there can be no attempt made to check the bleeding. As has been said, it is out of the question to use the ordinary means to bring about the necessary dilatations of the cervix, for the reason that they demand too great an expenditure of time and consequent loss of blood. In the light of the foregoing it will be evident that the cases of this group are proper subjects for the operations comprised under the term of accouchement forcé. I believe that the indications here are best met by the method of Bossi, pursued until a diameter of about 6 cm. is attained, and then followed by the so-called vaginal Cæsarean section, the operation of version, craniotomy or forceps being employed to deliver according to indications. I believe, however, if a case of the last mentioned group be met with under unfavorable circumstances, that it might be found better to deliver at once by abdominal Cæsarean section, since I am certain that the latter can be more safely carried out by a good operator, in the absence of good assistance, than can the former relatively more complicated method under unfavorable conditions. If done by the abdominal route I think that a hysterectomy should follow when possible as in many cases there is a marked degeneration of the uterine wall, with associated endometrial change.

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BONE CYSTS.

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Cysts in bone may occur in a variety of conditions, and are of interest not only from the standpoint of their etiology but also because since the discovery of the *x*-ray the diagnosis has been simplified and the reported cases more numerous.

Cysts have been reported as occurring in almost everyone of the bones. Those in the jaw arise as a result of errors in the development of the teeth or from persistence of the rudimentary enamel organ; these cysts have not been considered in the present paper. Cysts of the long bones are known to occur:

1. From parasites, the echinococcus, etc.

2. In osteomalacia.

3. In arthritis deformans, from softening of an inflammatory area of the bone in the neighborhood of the joint.

4. As a cystic degeneration of the entire skeleton of unknown origin.

5. From softening in solid tumors, sarcoma, enchondroma, myxoma, etc.

6. As simple benign cysts due to the softening of a *rest* of embryonic cartilege, or from softening of an inflammatory or hemorrhagic foci.

1. *Hydatid cysts* are occasionally found in the cancellous tissue of bones and resemble the benign bone cysts, both in symptoms and physical appearance, until the cyst has been opened at operation. They are very uncommon, however, the bones being affected in 3.5 per cent. only of the reported cases of echinococcus cysts.

2. In *osteomalacia* the rarefying osteitis may so widen the Haversian canals that cysts may be discovered accidentally by the *x*-ray or upon the occurrence of fracture or bending of the bone.

3. Ziegler especially, has called attention to the occasional

cyst formation in *arthritis deformans* supposed to be due to softening of the bone near the affected joints. These cysts differ from the benign bone cysts, in having a thicker layer of cortical bone surrounding them which would rarely lead to fracture. In a recent monograph by Grunert mention is made of the fact that no fractures from this cause have been recorded.

4. In 1864 Engel reported a much quoted case where all the bones were found to be the seat of cysts, and recently Heinecke has observed multiple cysts, which he believed were associated with osteomalacia. The disease has been termed *cystic degeneration of the entire skeleton*, and the origin of such cysts has not been made clear.

5. As a result of degeneration, sometimes of hemorrhage, cysts may form in certain tumors originating in the bones. These cysts, however, are quite distinct in their appearance from the benign cysts and can usually be distinguished from them. The rapidly growing round and spindle-cell sarcomas with extensive destruction of the cortical bone and considerable new bone formation need not be discussed, as the nature of the tumor should be recognized and amputation performed if feasible.

Giant-cell medullary sarcomas of bone must be classed separately, as the clinical course, and subsequent behavior after operation show them to be practically benign. A recent case reported in the BULLETIN, by G. G. Davis, illustrates such cysts. They resemble the simple cysts very much and while occurring later in life the diagnosis will often have to be decided by microscopic examination of the tissue forming the wall of the cyst.

A few years ago Jenckel recorded a cystic sarcoma arising from the lesser trochanter of the femur in a man aged twenty-two years, and containing venous blood. Simple enucleation was followed by freedom from recurrence. Such "blood cysts" are not uncommon in these medullary giant-cell sarcomas and are sometimes so prominent and so large as to constitute the so-called *bone aneurysms*, first mentioned by Percival Pott. A number of classic cases are on record in some of which it is evident that they were simply hæmatomas in a sarcoma.

König has described cyst formation in enchon-fibromas and reports such a tumor in the femur of a girl aged fifteen years. The symptoms were similar to those usually observed in the benign bone cysts, and the growth was believed to have originated from the epiphyseal line below the trochanter.

The cysts were thought to have resulted from the degeneration of areas of hemorrhage and a myxomatous softening of the cartilege. The complexity of König's case was due to the presence of considerable tumor tissue within the expanded shell of bone and surrounding the cysts, and which was composed not only of areas of cartilege but also of a connective tissue with many spindle cells and giant cells, which was not considered sarcomatous.

Nové-Josserand reported a cystic periosteal myxoma of the tibia in a boy of sixteen years, of three weeks' duration and believed to be of congenital origin. The growth was largely composed of mucous tissue and covered by thickened periosteum.

6. Benign bone cysts seem to have been first accurately studied by Virchow in 1876 from a case reported by him, and one which had previously been recorded by Froriep (1838) and restudied by Virchow. In 1884 Billroth discussed the etiology of these cysts and compared them with the normal cavities in the skull and with dentigerous cysts. But few cases however were recorded before the discovery of the *x*-ray, since which the number has multiplied. The following description is based upon one observed case, such others, forty-three in all, as could be found in the literature and especially with the aid of the excellent papers of Bloodgood, Schlange, König, Koch, and recently Haberer.

The following cyst was operated upon by Dr. C. H. Frazier in the University Hospital:

F. R., a student, aged nineteen years. Father died from carcinoma of the stomach; mother and one sister living and well; three brothers died from acute diseases. No venereal history.

In May, 1903, without trauma or other apparent cause the patient noted a swelling over the region of the fourth metatarsal, inflammatory in appearance but not painful unless subjected to direct pressure. During the months of June and July the tumor decreased in size only to reappear during August, and of firmer consistency. The size increased, pain was experienced, and during September he could walk with difficulty. Upon admission to the hospital, a fusiform swelling was felt involving the fourth metatarsal of the left foot having a smooth surface and not inflamed. An *x*-ray (see Fig. 1) revealed the tumor to be a cyst, although Dr. Pancoast stated that a central growth could not be excluded.

Operation consisted simply of disarticulating the fourth metatarsal. Recovery was rapid and uneventful. The patient has experienced no recurrence, three years after operation.

Pathological Report. (Surg. Path., No. 417.) Upon sawing the metatarsal bone longitudinally the cyst was observed as occupying the distal half and extending nearly to the joint cartilege. The cyst was about the size of a pigeon's egg (Fig. 2), contained a reddish-brown serous fluid and had expanded the cortical bone. The latter measured about two millimetres at the thinnest portion, and while easily bent did not give any crepitation. The inner wall was lined with a reddish soft tissue, ridged in some places and extending trabecular-like across the cyst. No areas of cartilege were

perceptible. No cultures were made of the contained fluid. The periosteum was normal in appearance.

Microscopically, the thinned cortex with its narrow bony trabeculæ and widened cancellous spaces indicating the atrophy of the bone are well shown in Figs. 3 and 4. Upon the cyst side the soft tissue mentioned in the gross description is seen to be active granulation tissue with abundant fibroblasts, bloodvessels with definite walls and interspersed with giant cells (osteoclasts). The periosteum is fibrous, without its osteogenetic layer, and the muscle is not involved even though the widening of the cancellous spaces is only limited by the periosteum. This case is so exactly like the description and drawing of the one described by Corson as to be

Fig. 1.—*x*-ray picture of cyst of fourth metatarsal bone.

remarkable. No areas of cartilage were detected after sectioning the entire half of the cyst. Including this case I have collected forty-four reported cases of bone cysts after excluding those of the jaw, called dentigerous cysts.

Locality. In four of the cases more than one bone was involved, and in one (Carle), reported in 1878, the forearm is mentioned as the seat of growth—with this exception there is reference made to fifty cysts in forty-three patients, of which thirty-eight (76 per cent.) were located in the three bones, most usually involved in any bone disease, viz., the femur (38 per cent.); the tibia (22 per cent.), and the humerus (16 per cent.). The remaining cases were scattered among the phalanges (three); the pelvis (two), and the fibula, radius, ulna, calcaneus, metatarsus, inferior maxilla, and parietal bone, one each.

In thirty-seven cases in which the fact is recorded, the right side was involved twenty-three times and the left fourteen.

Age and Sex. Excluding an isolated and peculiar case reported in 1889 by Westphalen, in which the patient was eighty-two years of age, the average of thirty-nine cases was twenty years (19.4). Expressed in decades:

1 to 9 years	7 cases.
10 to 19 "	20 "
20 to 29 "	6 "
30 to 39 "	3 "
40 to 49 "	2 "
50 to 59 "	2 "

It will thus be seen that 67.5 per cent. of the cases were under twenty years of age; 82.5 per cent. before the age of thirty. Of forty-one cases, twenty-two were in males; nineteen in females; sex apparently having no bearing upon the etiology.

Fig. 2.—Cyst of fourth metatarsal bone: *A*, thinned and expanded cortex. *B*, lining membrane, showing ridges.

Symptoms. There are four cardinal symptoms of this disease which stand out so prominently in the history of every case as to be pathognomonic if only a cystic sarcoma be excluded, pain, swelling, impairment of function and fracture upon slight trauma. The pain varies in its intensity, is often intermittent and is usually described as rheumatic in character; it may be the first symptom or may not be noted until after the appearance of the swelling or the occurrence of a fracture, it occasionally is absent as in Codman's, Buchanan's, and several other cases.

The swelling is due to the expansion of the thinned cortical bone by the increase in contents of the cyst cavity, and may be located to one side of the bone when the upper end of the femur is involved, or may be fusiform in shape in the case of the tibia, humerus, etc. Occasionally, as in Corson's case, no swelling is noted. Sometimes parchment crepitation (Depuytren) or ping-pong ball crepitation (Bloodgood) may be elicited.

Fracture occurs from slight trauma such as a misstep, a fall from a low chair, grasping the arm, etc., and curiously

in most of the reported cases, the bones reunited under treatment and the true nature of the lesion was only suspected by the subsequent occurrence of pain or swelling at the site of the old fracture. The duration of these cysts has been variously recorded as existing from several months to several years.

Diagnosis. As Bloodgood states, "the only medullary tumors of the long pipe bones which, in their growth, expand the bone and produce a definite shell, are the bone cysts, the myxochondrosarcoma and the giant-cell sarcoma." From the latter two a differential diagnosis may be attempted, but is often difficult until the interior of the cystic cavity is laid open at operation, but fortunately all of these lesions may be cured by a conservative operation.

cysts observed. These contain a clear or turbid fluid, yellow, red or brown, in color; serous or mucoid in character, the cyst varying in size from two to eight centimetres. The thined cortex is lined by a reddish brown soft tissue, scanty in amount and sometimes extending across the cyst in the form of trabeculæ or septa. In about half the cases cartilage may be noted as a tissue of a slightly bluish color.

Prognosis. Practically every case should recover after a conservative operation. Of the forty-four cases which I have collected, recovery took place in all but four; those of Froriep (1838), Körte (1880), and Westphalen (1889). A number of cases are on record as being free from recurrence several years after a conservative operation.

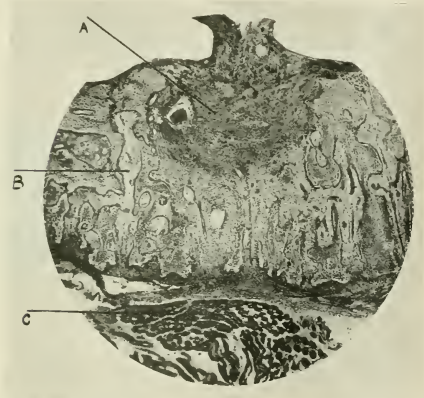

FIG. 3.—Photomicrograph (low power) of cyst wall: *A*, lining membrane composed of young connective tissue; the giant cells have been retouched in some places. *B*, rarefied cortical bone. *C*, periosteum and muscle.

FIG. 4.—Medium power drawing of wall of cyst: *A*, bony trabeculæ. *B*, soft tissue lining cyst, containing numerous osteoclasts, fibroblasts, and bloodvessels.

The bone cyst usually occurs before the completion of the diaphysis, but not always so; the sequence of symptoms is usually pain, lameness, fracture and swelling, although one of these may be absent; the *x*-ray may reveal a distinct encircling shell of bone surrounding a light central cavity, but as Helbing points out, this finding is not always as characteristic as Beck contends. The diagnosis, therefore, may be suspected but its confirmation must be sought by operating upon the supposed cyst and noting certain well-marked characteristics. At operation the tissues will be found to be normal and not infiltrated, the periosteum smooth and unchanged. The thin shell of cortical bone may feel soft to pressure, and upon opening it with knife or chisel one or more

Treatment. A conservative operation is always indicated with exposure of the cystic tumor, raising a "lid" of bone and with gouge and chisel thoroughly remove all of the lining membrane. The cavity may then be cauterized with carbolic acid, dried and either packed with gauze or filled with iodoform wax. A plaster-of-Paris dressing may be necessary to prevent subsequent fracture.

Etiology. The origin of the cysts is not at all clear at the present time, there being three theories of causation. Virchow, in 1876, advanced the idea that they were the products of a softening of a portion of cartilage from the epiphysis of the bone, this hypothesis being rendered probable from the finding of portions of cartilage in the wall of the

cyst in about 50 per cent. of the reported cases. Beck looks upon them as the product of an inflammatory atrophy similar to osteomalacia or rachitis and indicative of a disturbance of nutrition characterized by the production of a rarefying osteitis, and increased absorption of bone, finally leading to a disappearance of a part of the bone tissue. D'Arcis believes, with others, that the cyst is produced by slight trauma, causing a hemorrhagic focus and the subsequent production of a cyst.

In the case reported in this paper there was no evidence of rickets, no history of previous trauma, and no "islands" of cartilage in the cyst wall after removal, and the cases recorded in the literature vary widely in certain peculiarities of the lining membrane. In König's case large masses of cartilage were present; in Boström's second case connective tissue only; Buchanan records a cyst lined with serous membrane, and Sonnenburg's case had no distinct wall. In several of the reported cases the tissue was distinguished from giant-cell sarcoma with difficulty, and emphasis must be laid on the fact that the clinical course and gross appearance of these cysts are more essential to a correct diagnosis than the microscopic examination of the tissue.

When the majority of the cases are considered they will be found to conform to the description given in the earlier part of this paper, only occasionally as in König's, and in one of Schlange's cases will the cyst be found to be excentrically placed. Perhaps some of the cysts are due to the softening of misplaced cartilage, but it is more probable that certain inflammatory or nutritional disturbances within the bones will afford a better explanation of the majority.

In a case of osteitis deformans recorded by Küster, a cyst the size of a cherry was found in the midst of the fibrous tissue and it is possible that the fibrous proliferation (osteomyelitis fibrosa of v. Recklinghausen) which causes this disease is closely related to the etiology of the simple bone cysts. The interrelation between osteitis fibrosa, osteomalacia, rachitis, and the benign bone cysts is a very interesting one.

The following conclusions agree with those of v. Mikulicz:

1. Bone cysts are most frequently observed during the period of growth of the individual.

2. The long bones are most frequently affected, especially the femur, tibia and humerus.

3. Slight trauma is a fairly constant etiological factor.

4. Bone cysts can be cured by thorough curetting, and recurrence should not take place.

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STUDIES ON PHAGOCYTOSIS.

By D. H. Bergey, M.D.,

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Metchnikoff first called attention to the phagocytic powers of the leukocytes in 1885 by demonstrating that these cells are able to take up pathogenic bacteria and digest them. A great deal of evidence of the phagocytic powers of the leukocytes was collected and this evidence received general recognition as elucidating the question of immunity. How-

ever, when the anti-infectious nature of the blood plasma was more fully studied and its relation to natural and acquired immunity became better established, the phagocytic power of the leukocytes was less favorably regarded.

With the general dissemination of the ingenious exposition of the mechanism of immunity promulgated by Ehrlich, the phagocytic power of the leukocytes was more and more lost sight of, though from time to time Metchnikoff and his associates called attention to facts which demonstrated that the leukocytes bore some relation to immunity. Following the demonstration by Leishman (*British Med. Journ.*, 1902, vol. i. p. 73) of a method by which the phagocytic power of the leukocytes can be tested outside the animal body, and the elaboration of Leishman's method by Wright and Douglas (*Proc. Royal Soc.*, 1903, vol. lxxii. p. 357) the phagocytic influence in natural and acquired immunity has been studied by many investigators.

The recent studies in this field along the lines laid down by Leishman and by Wright and Douglas have shown that the leukocytes play a far more important part in immunity than was conceded to them several years ago.

The studies of Wright and Douglas have demonstrated that the leukocytes are incapable of taking up bacteria unless they have previously been acted upon by a substance occurring normally in the blood, the opsonin, which prepares the bacteria for phagocytosis.

A certain amount of opsonin exists in the body fluids of normal individuals. Following recovery from infection by certain types of bacteria specific opsonins are found in the blood in considerable quantities. These opsonins which occur in the blood as the result of acquired immunity are specific for the particular species of bacteria which has caused the infection just as in bacteriolytic immunity the amboceptors formed are specific for the organisms causing the infection.

The infections in which specific opsonins are formed are especially those caused by staphylococci, streptococci and pneumococci, diseases in which there is but little evidence of the formation of either antitoxic or bacteriolytic immunity.

In other infections, however, there is also found an increase in the opsonic power of the blood serum along with an increase of other immune bodies. In diphtheria, for instance, after recovery from the infection the blood serum is rich in antitoxin but at the same time there is also found a development of specific opsonin capable of stimulating the phagocytic action of the leukocytes upon bacterium diphtheriæ. In typhoid fever on the other hand, after recovery from the infection, the blood serum is rich in the specific amboceptor which is essential to the bacteriolysis of the typhoid bacillus, but there is also an increase of the phagocytic power of the leukocytes for the typhoid bacillus over that seen in normal individuals.

While the opsonins play an important role in practically all bacterial infections, it is especially in individuals recovering from infections by the group of septicæmia-producing organisms where the opsonic index is high. This fact gives us an insight into the mechanism of immunity in this type of disease which was lacking previous to the demonstrations by Wright and Douglas.

Metchnikoff and his associates claim that the phagocytic cells concerned in the destruction of the bacteria are the polymorphonuclear leukocytes or microphages, except that the spirillaceæ are taken up principally by the large mononuclear leukocytes or macrophages.

With the idea of ascertaining whether the polymorphonuclear leukocytes were concerned to an equal degree in the removal of different types of bacteria I conducted a series of experiments with peritoneal exudate derived from normal guinea-pigs after injections of aleuronat. This exudate is rich in polymorphonuclear leukocytes but also contains a considerable number of large mononuclear cells, principally endothelial cells. This exudate was mixed with equal quantities of 0.85 per cent. sodium chloride solution containing sodium citrate and then added to various bacterial suspensions, in equal proportions, in capillary tubes. These tubes were incubated at 34° to 36° C. for thirty minutes, when smears were prepared and the numbers of bacteria taken up by twenty leukocytes was estimated in the stained smears.

TABLE I.—MICROPHAGES AS PHAGOCYTES.

Culture.	1	2	3	4	5	6	7	8	9	10	Mean.
Bact. pseudodiph.....	0.7	0 4	1.0	1.5	4.3	2.8	0.8	0.4	1.1	0.5	1 46
Strep. pyog. urine	7.2	1.1	1.1	1.0	3.6	4.1	4.6	2.5	4.7	4.6	3.45
Strep. pyog. scarlet fever	4.4	0.4	2.2	9.0	6.4	3.8	1.1	3.8	4.3	3.7	3.91
Mic. pyog. albus.....	1.5	0.5	2.0	4.3	4.5	3.0	1.7	0.7	0.8	2.7	2.17
Mic. pyog. aureus.....	1.8	0.6	1.9	5.0	4.2	6.0	3.0	3 4	2 6	4.5	3.30
Mic. catarrhalis.....	1.5	8 2	0.4	9.2	4.0	6.2	1.5	3.1	2.6	2.3	3.90

The leukocytes in the peritoneal exudate of normal guinea-pigs do not appear to have a special predilection for any particular species of bacteria, though there is more or less constant difference as to the number of organisms taken up. For instance in a series of ten experiments with such exudate (see Table I.), the mean of the ten observations upon two strains of streptococcus, one of micrococcus pyogenes aureus, one of micrococcus pyogenes albus, and one of micrococcus catarrhalis shows that the results are fairly constant, while the number of organisms of bacterium pseudodiphtheriticum taken up is about half as great. There are, however, very marked differences between the results obtained with different animals for these several organisms. In part the differences in the results must be attributed to factors which it was impossible to fully control. For instance one important disturbing element that it was impossible to overcome in many instances is a very marked tendency for the leukocytes to adhere to the walls of the capillary tube and resist removal when the fluid is spread upon a glass slide. In this manner

no doubt numerous cells were lost in some of the experiments while in others there seemed to be less tendency for the cells to adhere in this way. Another factor which no doubt helped to influence the results is the extreme delicacy of the cells and their great liability to rupture on account of disturbances in osmotic conditions through the diluting fluids. This disturbance was not noticeable to equal extent in all of the exudates as it appeared to be more marked in some instances than in others.

In a second series of five experiments, in which micrococcus pyogenes aureus, microspira schuylkilliensis and bacillus dysenteriæ were the organisms employed, somewhat greater differences in the results were noticeable, in that micrococcus pyogenes was taken up in almost twice the numbers as compared with the other two organisms, as the mean of five observations shows. The mean of these five results, however, is very materially influenced by the fifth experiment in which the results were very much higher than in the other four. (See Table II.) Microspira schuylkilliensis in the first four experiments of this series appears to be especially insusceptible to the phagocytic action of the leukocytes, and moreover it was frequently very difficult to ascertain whether the bacteria were really within the stroma of the cells or were merely adherent to their exterior.

TABLE II.—MICROPHAGES AS PHAGOCYTES.

Culture.	1	2	3	4	5	Mean.
Mic. pyog. aur.	4.4	2.0	0.8	2.0	2.5	2.3
MeSp. Schuylkill.	0.5	0.1	0.15	.0	5.2	1.2
B. dysenteriæ	0.6	0.6	0.7	0.6	3.0	1.1

In general then the experiments seem to indicate that there is some degree of difference in the peritoneal exudate of normal guinea-pigs as to its power of inducing phagocytosis of different species of bacteria. We see this power more distinctly marked in the group of organisms producing septicæmia and manifested to a much lower degree in such organisms as schuylkilliensis and dysenteriæ, which induce infections characterized particularly by a bacteriolytic immunity, and in which an opsonic immunity is far less marked.

Another line of investigation was also pursued at the same time, and that was to ascertain to what degree the large mononuclear cells were concerned in phagocytosis for the same organisms. With the peritoneal exudates of the ten guinea-pigs in Table I., and with the same organisms employed for the tests recorded in this table, similar observations were made upon the number of bacteria taken up by the macrophages. With regard to the phagocytic powers of these cells the means of the ten observations indicate that though these cells are present in far smaller numbers they have the power of taking up greater numbers of bacteria in the same length of time; in some instances almost three times as many bacteria having been taken by the macrophages as compared with the microphages. There appeared to be no marked constancy in these results obtained for the microphages. (See Table III.) These results are based on the enumeration of the bacteria contained in five of this class of cells.

TABLE III.—MICROPHAGES AS PHAGOCYTES.

Culture	1	2	3	4	5	6	7	8	9	10	Mean.
Bact. pseudodiph.	1.3	0.4	16.2	9.4	6.3	5.0	2.6	1.7	4.4	1.3	4.86
Strept. pyog. urine	3.7	6.2	10.7	4.3	1.6	6.9	4.4	4.1	15.0	15.0	7.19
Strept pyog. scarlet fever	21.4	5.0	2.4	4.0	2.1	3.4	5.4	1.6	5.3	12.2	6.78
Mic. pyog. albus	3.2	0.4	5.5	3.3	2.3	8.9	5.6	1.2	0.6	3.1	3.41
Mic. pyog. aureus	7.4	7.5	0.8	15.0	4.1	4.3	3.2	21.2	4.0	15.4	8.29
Mic. catarrhalis	2.9	1.1	0.6	3.0	1.9	18.7	4.4	6.5	2.0	4.0	4.51

In the second series of five experiments there is evidence to believe that the macrophages have a more definite phagocytic power for the spirillaceæ than for other bacteria, because in this series of tests the mean for schuylkilliensis is distinctly higher than for the other two organisms, though in one of the tests a negative result is recorded, but this may have been one of those instances in which osmotic disturbances have caused rupture of this class of cells. (See Table IV.)

TABLE IV.—MICROPHAGES AS PHAGOCYTES.

Culture	1	2	3	4	5	Mean.
Mic. pyog. aur.	7.2	2.0	1.6	2.5	0.5	2.8
MeSp. Schuylkill.	8.6	0.6	.0	2.6	6.2	3.6
B. dysenteriæ	3.0	.0	2.3	.0	3.0	1.7

Though the results obtained with the exudates derived from different animals show marked variation as to the phagocytic powers of the leukocytes for the several reasons stated, the procedure is of importance from the fact that when we take the mean of a number of observations the results show a fair degree of constancy. The difficulties encountered in this investigation are such that are less likely to occur in the ordinary procedure of determining the phagocytic powers of leukocytes in blood. Although sodium citrate salt solution was employed for purposes of dilution it did not seem to overcome the difficulties named. It seems possible that the original Leishman method will give more satisfactory results with such exudates than will the modification of Wright and Douglas which I employed, though no experiments were made to substantiate this statement.

The following conclusions seem to be warranted from the results of the investigation:

1. The polymorphonuclear leukocytes have a distinctly greater phagocytic power for certain bacteria than for others. This phagocytic power is especially high for the group of organisms inducing septicæmic infection and less so for other bacteria.

2. The large mononuclear leukocytes, that is, the large lymphocytes and endothelial cells derived from the peritoneal surfaces, have a distinctly greater phagocytic power for bacteria than do the polymorphonuclear leukocytes. This appears to be especially the case with the spirillaceæ.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

ABSCESS OF THE BRAIN.[1]

By William G. Spiller, M.D.,
Professor of Neuropathology and Associate Professor of Neurology in the University of Pennsylvania.

(From the Department of Neurology and the Laboratory of Neuropathology in the University of Pennsylvania.)

The diagnosis of cerebral abscess depends chiefly upon the signs of some more or less rapidly developing lesion of the brain, with the discovery of a purulent process in the body, or of a wound of the head. Abscess of the brain without any evidence of pus elsewhere may be extremely difficult to diagnose. The cerebral signs are much the same as those of tumor of the brain. The choked disc may occur in either condition, but is more likely to be intense in tumor and to occur earlier, but I have observed choked disc of high grade in abscess.

The temperature and pulse are likely to be subnormal in abscess, but they may be normal or even above normal, especially if the abscess is complicated by meningitis. We should not depend too much on the condition of the pulse and temperature. The temperature is more likely to rise in the terminal stage of abscess, but a rise may occur at any period and be caused by the primary suppurative process, as a superficial wound or purulent pulmonary disease. The stupor, in my experience, is usually greater in advanced stages of abscess than in tumor, and yet an abscess may be latent or nearly latent a long time, and stupor may be pronounced with brain tumor. It is not uncommon to find slow cerebration preceding stupor in either condition. In many cases the diagnosis must be in doubt; but given a case of long-standing purulent otitis media, with recently developed signs of disease of the temporal lobe or cerebellum, the diagnosis of abscess becomes more positive. High leukocytosis speaks in favor of abscess or purulent meningitis in contrast with tumor. Where the cerebral symptoms appear after a purulent pulmonary process the diagnosis between tumor and abscess of the brain is difficult. Virchow is said to have been the first to call attention to the frequency of abscess following a purulent affection of the lungs. Still more difficult is the determination as to whether purulent meningitis or brain abscess is present, and often the two conditions are associated in the same person. The diagnosis is important, because less can be hoped for from operation if purulent meningitis develops, whereas operation is demanded if the condition is one of abscess. Lumbar puncture[1] is of great value, as pus in the cerebrospinal fluid obtained by this means points to purulent meningitis; but purulent meningitis may exist although pus in the spinal fluid is not obtained. The presence of mononuclear or polynuclear cells in the cerebrospinal fluid is also of diagnostic value. Kernig's sign is of value as indicating meningitis, but is not pathognomonic, and may occur with abscess. Rigidity of the neck is more likely to occur in meningitis, but may occur with abscess. Where abscess is associated with purulent meningitis the prognosis is extremely grave.

The following case shows how difficult it may be to decide between cerebral abscess and cerebral hemorrhage:

A man, about forty years of age, was admitted to my service at the University Hospital, in an unconscious condition, March 20, 1906. No history was obtainable, except that he was known to be a chronic alcoholic, and had been unconscious on several occasions. He had been found in a stable, and brought from there to the hospital. No signs indicating an injury could be detected.

I examined him March 21. He had conjugate deviation of head and eyes to the left, and paralysis of the right upper and lower limbs. The temperature was above normal, 101°, and on one occasion 103°, until March 26, and remained normal until April 27, when it rose to 101°; it fell again to normal on April 30. I supposed the man had probably had a hemorrhage of the brain. No discharge from the ear was present. He improved somewhat, but never spoke. A copious purulent discharge from the left ear began April 28. His condition had improved by this time to such a degree that a more thorough examination could be made. He was still completely paralyzed in his right limbs and right side of his face; he had diminished sensation of pain on the right side, and had also right hemianopsia. He was evidently word deaf, and could not speak. He had a leukocytosis of 16,640. Lumbar puncture allowed 30 c.c. of perfectly clear fluid to be withdrawn, but a smear preparation of the sediment showed no cells. Kernig's sign and rigidity of the neck were not present.

[1] Read by invitation before the Allegheny County Medical Society at Pittsburg, May 15, 1906.

[1] An excellent presentation of lumbar puncture has recently been made by Kopetzky, Amer. Jour. of the Med. Sciences, April, 1906, p. 648.

Dr. Randall examined the ear and expressed the opinion that the discharge was caused by chronic suppurative otitis media and that it did not contain cerebrospinal fluid. There seemed to be no mastoid involvement.

Dr. Carpenter, in Dr. de Schweinitz's clinic, examined the eyes and reported that the man had bilateral neuroretinitis with hemorrhages. The swelling of the disc was not marked and the fundus disturbance was rather widespread. The veins were very much swollen.

On account of the purulent otitis media, the leukocytosis, the neuroretinitis, the symptoms pointing to a lesion in the left first temporal convolution and extending to the internal capsule and optic radiations (right hemiplegia, hemihypalgesia, hemianopsia, word deafness), I feared the patient might have a cerebral abscess, and requested Dr. Frazier to operate over the left first temporal convolution. A subdural hemorrhage was found in this region. The otitis media and the hemorrhage on the brain were probably the result of trauma. Had there been no otitis media the opening of the skull probably would not have been made, as the symptoms otherwise seemed to point to an inoperable intracerebral hemorrhage. The patient died two weeks after the operation, and a large hemorrhage was found within the left basal ganglia.

Headache and vomiting are common and early signs of abscess or tumor of the brain. Chill is a common symptom of abscess, and likewise is general muscular wasting, if the patient lives sufficiently long. Frequent yawning is not uncommon with brain abscess or tumor. I have seen it a number of times, and occurring as it does, when the patient is in marked stupor, it is a striking sign.

As an example of an unusual method of infection of the brain, I mention a case described to me by Dr. B. A. Randall. A boy was tossing up an umbrella, when one of the ribs penetrated the ethmoid bone through the nostril and caused cerebral abscess.

Abscess of the brain or purulent meningitis may readily occur in association with a purulent thrombus of the lateral sinus secondary to otitis media. Indeed, these conditions are sometimes produced in this way, although sinus thrombosis is not the most common cause of abscess. More frequently the infecting organism is carried directly into the brain substance. The diagnosis as to whether or not abscess complicates sinus thrombosis is of great importance, because it is desirable to leave the dura unopened if it can be done with safety. I have seen a case under the care of Dr. B. A. Randall (Case I) in which this question arose. The notes are given in detail further on.

The right external jugular vein and some of its tributaries were ligated two inches below the angle of the jaw, by Dr. Randall, on account of thrombosis and the part above removed. The right lateral sinus was thrombosed. It was opened, the thrombus removed, and the sinus packed. The right ear had discharged purulent fluid for four years. Dr. Randall invited me to see the patient after this operation. The boy was in marked stupor, but could be aroused to answer questions. The pulse was about 65 and the temperature was normal. The patellar reflexes were absent. He had had some ataxia of his left limbs, but had not had any weakness of his limbs nor the Babinski sign. The symptoms were suggestive of cerebellar abscess, and the question therefore became very pressing as to whether the dura should be opened or not. The symptoms after the operation on the lateral sinus and jugular vein were very grave, but in the opinion of Dr. Randall and myself might be explained by the lesions already found, and to open the dura through an infected region would expose the boy to grave danger of intradural infection. The latter might be avoided by sterilizing the dura at the point of operation, and later by packing with iodoform gauze; but the penetrating powers of micro-organisms is great, and we were eager to avoid the risk of adding any complication in the serious condition of the little patient. Delay was therefore decided upon. The symptoms were carefully watched with the idea that any increase in them would justify the opening of the dura and searching for an intradural abscess. Just here I may remark that judicious delaying is one of the most difficult problems of cerebral surgery. Our course was justified, the patient slowly improved, and a few weeks ago I had the pleasure of seeing him in very good condition.

E. W. Roughton,[1] in reporting a case of cerebellar abscess, recently says: "Let me now tell you that much more severe and definite symptoms of intracranial disease may occur in cases where, so far as one can judge, there is extensive disease of the ear and mastoid process without any actual disease inside the skull; perhaps one is not justified in stating that there is no intracranial disease in these cases, but it is certain that they may recover after operative treatment limited entirely to the ear and mastoid process." He refers to the case of Sainsbury and Battle, in which the symptoms were severe, and constant headache, drowsiness, frequent vomiting, giddiness, inequality of pupils, diplopia, well-marked double optic neuritis, and pyrexia of an irregular type were present. Mastoidectomy was performed and the patient recovered completely. The cranial cavity was not opened. These writers believe that in all cases of ear disease with head symptoms sufficiently grave to call for operative interference, and including even a severe optic neuritis, the patient should not be subjected to the major operation of craniotomy until the minor operation of clearing away all extracranial disease has been performed. I would urge, however, that the delay should not be long, as the symptoms mentioned above are very important.

[1] Lancet, 1905, vol. ii, p. 1597.

It is astonishing that purulent otitis media may exist a long time and not cause brain abscess until after many years. Oppenheim speaks of a case in which the otitis media existed thirty-four years, and of another in which it existed forty-five years before abscess developed, and yet acute otitis media may cause abscess. According to Grunert, in 91 per cent. the process is chronic, in 9 per cent. acute. Schmidt and Gruber have reported cases in which the ear disease seemed to be cured before a brain abscess developed, and on the other hand Baginsky and Gluck have observed a case in which signs of brain abscess appeared on the twenty-second day after the commencement of the ear disease (cited by Oppenheim). I have had the opportunity of observing with Dr. Randall a case in which a temporal lobe abscess developed in a man sixty-eight years old (Case II), who had had middle ear disease most of his life. As the symptoms of brain abscess began only a few weeks before his death, it does not seem probable that he had had a latent abscess for a long period of time. Before the operation on the brain the pulse was 102 and the temperature 99° and a fraction; but this man did not have meningitis and had two abscesses near together in the temporal lobe, probably parts of one lesion, only one, however, was found at the operation and evacuated. The elevation of the pulse and temperature when I saw him was late in the disease, and this is sometimes the case in abscess.

Oppenheim, probably the first, has called attention to the occurrence of hemorrhagic encephalitis as the result of otitis media. The symptoms are likely to be those caused by lesions of the motor cortex.

Multiple abscesses make operation very uncertain, as there is no means of determining from the symptoms whether the patient has one or several abscesses, possibly communicating, and abscesses often are multiple. Abscess of the brain not infrequently is multilocular, and one or more pockets may escape detection, as in the case referred to above (Case II). Another difficulty the surgeon has to contend with is unusual density of the pus. In one of the cases I had the opportunity of studying with Dr. Randall the diagnosis of cerebellar abscesses seemed sufficiently clear to justify operation. This was done by Dr. Randall. The patient's temperature before operation was about normal; her pulse ranged from 64 to 108. Unfortunately the notes have been mislaid. She had lateral nystagmus in looking toward the side of the cerebellar abscess, and this sign I believed might be of value in determining the affected lobe, but I have not been able to find it in any other case, although I believe it has been observed a few times by others. The necropsy showed that Dr. Randall must have entered the abscess with the trocar, and yet no pus flowed. The lesson to be learned from this case is that the brain or cerebellum should be incised and not merely punctured at the place suspected of concealing an abscess, as little damage is done to a lateral lobe of the cerebellum by incision if the wound does not become infected; indeed, the cerebellum seems to be able to stand much rough handling, even the excision of a large part of a lateral lobe, without causing serious symptoms, as we have seen in a number of cases at the University Hospital.

Most of the cases of brain abscess I have collected for this paper have resulted from middle ear disease, but a case reported by Dr. C. K. Mills and myself, in 1896, was without discoverable primary lesion at the necropsy. The primary focus may produce no clinical signs.

C. H., a baker, forty-eight years of age, was admitted to the hospital January 30, 1896. He had previously been in fair health. His mother had never heard him complain of earache. During the summer of 1895 he suffered constantly from severe headache.

On December 20, 1895, he became unconscious and had three general convulsions. He remained unconscious two days, and when he regained consciousness it was noticed that he was partially paralyzed on the right side, and that he could not talk properly.

January 29, 1896, he had another attack of unconsciousness without convulsions, but with aphasia and paralysis. He was brought to the hospital next day. On admission he was in a condition of stupor; he did not speak when addressed and had almost total right-sided paralysis, incontinence of urine and feces, and entire loss of pain and touch sensations over the paralyzed side. By testing him with food brought toward his mouth from the right or left side it was noticed that he opened his mouth to receive the food only when it was brought from the left side. Likewise, when a pointed instrument was brought near either eye from the side, as if to touch it, he winked only when the motion was made in front of the left half of each eyeball. From these tests it was evident that right homonymous hemianopsia was present. He was found to have double papillitis, more marked in the left eye. His general condition gradually became worse. He occasionally complained of headache, which he did not localize.

On February 25, 1896, breathing was stertorous and the face dark red in color. The coma gradually increased until he died, twenty hours after the beginning of this attack. There was no evidence at any time of middle ear disease. During the entire time he was in the hospital, until just before death, respiration, pulse, and temperature presented no indications of the purulent process within the brain.

A horizontal section made just above the corpus callosum revealed an abscess on the left side in the centrum semiovale, and corresponding anteroposteriorly with the position of the optic thalamus, internal capsule, and part of the lenticular body. Both tympanic membranes were normal. No evidences of suppuration or perforation were present. The

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pleura, pericardium, heart, spleen, and kidneys were normal.

Microscopic examination of the pus from the cerebral abscess showed only the ordinary staphylococcus pyogenes aureus. There were about two ounces of pus in the abscess cavity and left ventricle. Both eyes were removed and examined by Dr. Oliver, and the posterior halves of the eyeballs showed well-marked choked discs, more decided on the left side; the swelling and inflammation of the nerve head and surrounding retina were extensive and covered at places with minute capillary hemorrhage.

The right hemiplegia and right homonymous hemianopsia made a diagnosis of some lesion at the posterior part of the left internal capsule probable. The convulsions may have been caused by rupture of the abscess into the left lateral ventricle. The patient seemed to be word deaf.

As cerebral abscess may occur after suppurative processes in the lungs, these organs were examined, but nothing was found, with the exception of spots of catarrhal pneumonia in both lungs. Suppuration was present only in the cerebrum.[1]

One of the cases coming under my observation, the clinical history and pathological material of which I have obtained from Dr. Chas. S. Potts, under whose care the patient was, shows that a cerebellar abscess may readily escape detection (Case III). The temperature varied very little from the normal, but the pulse was a little high. The patient was a man, aged fifty-seven years, somewhat dull mentally, and had been unable to walk for a year on account of vertigo, and had complained of headache about four months, and had ataxia in walking. He was in semi-coma two days before his death. Ear disease was not suspected, and there was little reason for a diagnosis of brain abscess; and yet a large and small abscess near together were found in the left cerebellar lobe. The posterior inferior cerebellar artery passing to this lobe was dilated and thrombosed, and it was evident that in this way the abscess had originated. While the abscess in this case was not entirely latent, the symptoms were not sufficient to justify a diagnosis during the life of the patient.

Cerebral abscess is usually regarded as more common than cerebellar, and as Henri Bourgeois[2] says, this may be because the latter is less often diagnosed, and less often operated upon; but I doubt the correctness of this statement. He refers to the statistics of Acland and Ballance, taken from the records of St. Thomas' Hospital from 1876 to 1894, and according to these, nine abscesses were in the temporal lobe and seventeen in the cerebellum, and two of the latter were associated with temporal lobe abscess. The same investigators have found that at the Hospital for Sick Children in thirty-five years two abscesses of the temporal lobe and four of the cerebellum occurred.

Oppenheim[1] says that Pitt in 9000 necropsies found brain abscess in 56, of these 18 arose in the ear or temporal bone. Freitel in 6000 necropsies found abscess twenty-one times, and of these seven arose in the ear. Others regard one-half or more of the cases of brain abscess as arising in the ear. Gowers puts it at 42.5 per cent. Men have abscess two or three times as often as women. Le Fort and Lehmann's statistics of 458 cases of brain abscess are: Cerebrum, 327; cerebellum, 113; cerebrum and cerebellum, 11; pons, 5; cerebral peduncles, 1; fourth ventricle, 1. So that the relative frequency of cerebellar abscess to temporal lobe abscess is as one to three. Dr. Randall informs me that in his experience cerebellar abscess has been more frequent than cerebral.

Case IV, recently under my observation, shows how exceedingly difficult it may be to diagnose between abscess of the brain and purulent meningitis. A young man was admitted to my wards at the Philadelphia General Hospital, in marked stupor and paralyzed on the left side of the body. The temperature varied from 98.6° to 102° and was never subnormal; the pulse varied from 80 to 110; the respiration from 20 to 25, or occasionally 30. Cerebrospinal fluid obtained by lumbar puncture showed lymphocytes 4 per cent., but no organisms. Within a few days he was found to have a purulent discharge from his right ear. The diagnosis seemed to be abscess of the right temporal lobe, implicating the right internal capsule and thereby causing left hemiplegia, possibly associated with purulent meningitis, and secondary to otitis media. Dr. E. Laplace, whom I called in consultation, and I decided that the patient was unable to endure an operation. A day or two before his death rales were heard in the lungs. He had no abscess of the brain, but the upper part of the right cerebral hemisphere was covered with pus, as was also to a less extent the corresponding part of the left hemisphere; pus was also found at the base of the brain and in the lateral ventricles. Cultures taken at the necropsy revealed tubercle bacilli, and miliary tuberculosis of the lungs was found.

Case V, studied by Drs. Hoyt, Randall, Frazier, and myself, shows how difficult the diagnosis of cerebral abscess may be. The slight elevation of temperature suggested purulent meningitis; the slightly subnormal pulse, abscess; both, however, might indicate abscess. The presence of pus in each ear and in the nasal sinuses without localizing cerebral symptoms made the diagnosis of location difficult, but the marked stupor left no doubt in our minds that some intra-

[1] Mills and Spiller, Journal of Nervous and Mental Disease, September, 1896.

[2] Contribution a l'étude des abcès otitiques du cervelet. G. Steinheil, Paris, 1902.

[1] Der Hirnabscess, Nothnagel's System, Band ix, Theil 11.

cranial lesion was present, and we believed that it was purulent chiefly because of the purulent processes in the bones of the skull. Optic neuritis, so valuable a sign of tumor or abscess, was not present. The pain was confined to the left temporal region, but this was an unreliable sign, for I have known localized pain of the head to be very misleading. However, because of its presence on the left side, and the more serious middle ear disease on the left side, the operation was performed on the left side. We fully recognized that the abscess might be in the right temporal lobe. The absence of word-deafness in this case did not alter our diagnosis, as abscess in the temporal lobe is usually in the lower part of the lobe and below the centre for word-hearing. In a left-handed man, as the patient was, it would not be likely to cause deafness even if it extended into the first left temporal convolution.

Dr. Hoyt, who first had charge of the case, and performed the necropsy, believed from the findings at the necropsy that the purulent meningitis was of recent origin, and the question arises, Could it have been caused by the free irrigation of the abscess cavity and the washing thereby of some of the infectious material into the meninges. [Much flocculent meningeal fluid was found before the abscess was irrigated.] An abscess cavity possibly should be irrigated, but there is danger thereby of producing a purulent meningitis. Aspiration would be a dangerous proceeding, as often the pus would not be thoroughly evacuated and in some cases would not flow freely through the needle. It seems well to avoid very intense irrigation of an abscess cavity, and it is possible that drainage with moderate irrigation would be sufficient, especially if after the operation the patient is made to lie with the opening downward, so that the pus may find free escape. Dr. Müller has suggested to me that sponging out the abscess as is done in the abdominal cavity might be sufficient.

Unusual and interesting cases of brain abscess are the following: A case of brain abscess with cure was reported by Randall and Potts[1] in 1903. After removing pus from the mastoid cavity a perforation of the dura, 2 mm. in width, was discovered, out of which pus was escaping. An incision through the dura exposed the brain substance, which showed no appearance of intracerebral abscess, but a few days later such an abscess was found and evacuated. A few days still later another abscess cavity was evacuated. The child recovered. There seems to have been a limited subdural abscess in this case associated with multiple intracerebral abscesses, and yet recovery occurred.

Pial abscess is uncommon, but Randall[2] reported a case in 1894 in which in association with extensive meningitis a small abscess cavity was found lying between the medulla oblongata, pons, and cerebellum; a smaller abscess occupied the corresponding position on the right, while a third, much larger, was found above the medulla oblongata. These three abscesses were within the pia. In this case the pulse was slow when the temperature was high. This case resembles an unpublished case seen by Dr. T. H. Weisenburg, whose specimens I have seen.

The brain abscess is likely to be on the side of the middle ear disease and near the petrous portion of the temporal bone, but in some cases the discharging ear may not be the primary focus, and the other ear may have been the longer and more seriously affected, although at the time of observation there may be no discharge from this ear. In a case (Case III) reported by Stoll[1] the abscess was secondary to an acute otitis media, and was situated in the parietal lobe. The author gives as an explanation for this unusual occurrence that the infection must have been embolic in character, and the embolus so small that it was not arrested until it had wandered some distance from its origin.

Abscess of the brain developing in the course of typhoid fever has been observed by A. C. Brown,[2] and his seems to have been the first case of cerebral abscess caused by this disease. The lesion was supposed to be a tumor, and operation resulted in evacuation of the pus and recovery. McClintock[3] has reported brain abscess caused by the typhoid bacillus.

The cause of death in operations on cerebellar abscess, according to Barr and Nicoll,[4] in many cases is thrombosis of the veins of Galen, with distention of the ventricles and œdema of the brain. The fatal result may rapidly follow the operation or may be delayed for weeks or months, even when recovery from the effects of the abscess is supposed to have occurred.

Abscess following trauma of the head without injury of the skin and bone of the head may occur. Ehrnrooth[5] has reported such a case. Intracranial hemorrhage certainly may occur from trauma without fracture of the skull, and probably a damaged portion of the brain may offer a favorable soil for the growth of bacteria, but nevertheless bacteria must penetrate in some way.

Cassirer[6] has found reported in the literature sixteen cases of abscess of the pons and medulla oblongata, but of these only ten seem to him trustworthy. Two, or possibly three, were cases of abscess of the medulla oblongata; in the others both pons and oblongata, or pons alone, were implicated. He himself has reported a case. The reasons for the infrequency of abscess in this part of the brain, according to

[1] Archives of Otology, 1903, No. 3, vol. xxxii.
[2] The University Medical Magazine, June, 1894.

[1] American Journal of the Medical Sciences, February, 1906, p. 223.
[2] Edinburgh Med. Journal, new series, 1900, vol. viii, p. 228.
[3] American Journal of the Medical Sciences, April, 1902, p. 595.
[4] British Med. Journal, February 16, 1901, p. 390.
[5] Deutsche Zeit. f. Nerv., vol. xx, Nos. 1 and 2, p 103.
[6] Archiv. f. Psych., vol. xxxvi, No. 1, p. 153.

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Cassirer, are the relative smallness of these parts, the less liability to injury, and the remoteness from the various cavities of the skull from which the primary infection comes. If a septic embolus is carried to the brain it is more likely to lodge in the left Sylvian artery. Possibly also the pons and medulla oblongata are more resistant to bacteria, as some have thought.

Abscess in each temporal lobe has been observed by Whitehead.[1] One abscess in the left temporal lobe was evacuated and eighteen months later the patient was well, but later cerebral symptoms developed. An operation revealed an abscess in the right temporal lobe, and this abscess was drained and recovery from the second operation also occurred. The patient had had a purulent discharge from each ear.

An interesting paper on cerebral abscess, which I read after my paper was completed, has recently been published by M. Allen Starr.[2]

RECORDS OF CASES.

In publishing the abbreviated records of the following cases I wish to thank my colleagues for permission to make use of their notes in connection with my own, especially Dr. B. A. Randall, with whom many of the cases were seen.

Case I.—*Sinus Thrombosis, with Symptoms of Brain Abscess.* (Service of Dr. Randall.) Philip W., aged fifteen years. *Chief Complaint.* Purulent discharge from middle ear followed by dizziness, headache, drowsiness and stupor with pain, induration, tenderness, and œdema over an area extending two and a half inches below the mastoid tip.

Four years ago he was struck over the right ear. Every winter since then he has had some discharge from his middle ear of a purulent nature. Two weeks ago this came on again as usual. Five days before admission he became suddenly dizzy and was obliged to take to his bed. He complains somewhat of pain below and behind the right ear, and has been in a semi-stuporous condition since, although able to answer questions intelligently.

Condition on Admission. Pupils are dilated and equal. Eye-grounds negative. Foul, light yellowish discharge from the external auditory meatus. No swelling, pain, or tenderness over the mastoid. Below and behind the mastoid extending down the neck there is an area (about two inches in diameter) which is tender, indurated, and œdematous. No pain in mastoid on percussion. Left hand and arm are slightly ataxic. Knee-jerks absent. Power in the arms and legs seems normal. No Babinski; no ankle clonus; leukocytes, 28,320.

Operation, December 4th. Under ether anesthesia, Dr Randall at 12 M. made an incision over the right external jugular vein; it was found to be thrombosed down to a point two inches below the angle of the jaw where it was ligated, as were also some tributaries. The wound was closed with gauze drainage. An incision was then made over the mastoid down to the lateral sinus. The bone was much sclerosed, but bled freely. The sinus was found large, thick, and thrombosed. It was opened, the thrombus removed, and the sinus packed after considerable difficulty; no pus was found. The middle ear was entered through the antrum and through-and-through drainage established. After thorough packing the wound was closed.

December 12th. Since operation he has been somewhat stuporous and apparently sleeping most of the day. His pulse remains steadily about 65. Temperature normal. Reflexes persistently absent. Upper portion of wound in neck is discharging a thin yellow fluid. Some induration in neck. He is nervous and irritable and his appetite is capricious.

Blood Count. Hæmoglobin, 55 per cent.; red blood corpuscles, 3,290,000; white blood corpuscles, 14,720.

December 18th. He has been steadily improving, does not sleep nearly so much; has been kept in sun parlor; is now sitting up; temperature normal, pulse rising, although still full. Appetite is good, sleeps well; knee-jerks, however, are persistently absent.

December 23d. Is now sitting up in a chair; wound does not pain. He is dressed every other day; seems much brighter and is gaining weight. Full recovery ensued.

Case II.—*Otitis Media of Long Standing, Symptoms of Brain Abscess of Short Duration.* April 17, 1901. Notes made by me in consultation on a case under the care of Dr. Randall. C. A., age sixty-eight years.

About January, 1901, the right ear was operated on by Dr. Randall and much pus and cholesteatoma masses were removed. Following this operation, and possibly before it, his mental condition was abnormal; he was, as expressed by one who had long known him, childish, but not irritable. His family have noticed for some weeks that the movements of the left face were somewhat impaired. About ten days ago the first signs of a distinct gradually developing paralysis was observed without apoplectic attack, in the left side of face and left upper and lower extremities. This paralysis never became complete. He dragged the left lower limb in walking. Yesterday he was in stupor for the first time, but was aroused when Dr. Randall visited him and he talked rationally for some time; he then went into stupor again and has remained in this condition since. He only once complained of feeling somewhat chilly. During the past week he has had considerable frontal and occipital headache, but no vomiting and no distinct vertigo or ataxia. I saw

[1] Lancet, February 13, 1904, p. 428.
[2] Medical Record, March 10, 1906.

him this afternoon (April 17th) and found him in profound stupor, so that he could not be aroused. The right limbs were moved voluntarily, but the left were only imperfectly moved. Involuntary jerking movements were seen in the left toes and left fingers, suggesting, in connection with other symptoms, irritation of the central motor tract. The left upper and lower limbs were very spastic. The reflexes in the upper and lower limbs were increased on both sides, but were checked somewhat by the spasticity of the left limbs. The left knee-jerk was more exaggerated than the right. The Babinski reflex was present on each side, but more marked on the left side. The left pupil reacted promptly to light. Hemianopsia could not be tested for on account of the stupor. The limbs were withdrawn when they were stuck with a pin, but the left upper and lower limbs were not so freely moved. Yawning was very frequent. No rigidity of head was noticed. Pulse 102, just before operation was 120; temperature, 99°. Neither side of the face was drawn. He never had slowness of pulse.

Dr. Randall adds to my notes that the patient had come under his care January 9, 1901, with chronic suppuration of the right ear, attic caries and cholesteatoma, having been long under Dr. Risley's care. Exenteration of tympanic cavities at the University Hospital, January 12, 1901; discharged, February 2, 1901, from hospital with wound healed and cavities dermatizing. Progress soon halted. Some weakness of left arm and mental slowness developed about March 10, 1901, previous to which he went about freely. These symptoms increased and on March 16th he became unconscious. A cerebral abscess in the sphenotemporal lobe was evacuated the evening of March 17th. He did not recover consciousness; the wound was dressed on the 19th and finger sought further abscess in vain. He died March 20, 1901.

Autopsy showed second abscess adjacent.

Case III.—*Cerebellar Abscess from Occlusion of Posterior Inferior Cerebellar Artery, Unrecognized during Patient's Life.* H. R. was admitted to the service of Dr. C. S. Potts, in the Philadelphia General Hospital, July 18, 1904, and died August 22, 1904, aged fifty-seven years. Dr. Potts' notes, August 20, 1904, are as follows:

Family History. Patient states that six months ago his hair began to fall out. Two months after this he began to have headaches, which persisted throughout the day. He also noticed about this time some difficulty in walking; he would stumble occasionally. At times he would have pains throughout the body.

He seems somewhat dull, but answers questions. He has been unable to walk for the past year on account of attacks of giddiness. He complains of headache. The left pupil reacts to light and in accommodation. No paralysis of the cranial nerves is found. The upper and lower limbs are normal in strength. He states that except for attacks of giddiness he can walk well. Knee-jerks and tendo Achillis jerks are present and normal. The plantar reflex is present, but not active, though all the toes flex. Sensations to touch and pain are normal. Stereognosis is preserved. He touches the tip of the nose with the index finger of either side very awkwardly.

Duration of illness two days.

Symptoms. Semi-comatose state; headache, backache, inco-ordination; throat and skin dry; polyuria; constipation; epigastric pain; coldness of hands and feet; always thirsty.

Autopsy. August 23, 1904. Embolism and aneurysm of left posterior inferior cerebellar artery; fibrosis of left cerebellar hemisphere, two abscesses of the left cerebellar lobe.

Case IV.—*Tuberculous Meningitis Causing Symptoms of Brain Abscess.* Christian Grandin, aged twenty-six years; white; was admitted to the Philadelphia General Hospital, December 27, 1905, and came into my service January 1, 1906. Died January 17, 1906.

Chief Complaint. Left hemiplegia.

Present Illness. About five weeks ago he complained of weakness in the left arm and leg. This weakness was irregular in its duration and would come and go. Sensation was also lost at times. Finally, about a week later, he was compelled to go to bed, but complete loss of power did not occur until one week ago, at the same time the mind became affected. The brother says that the patient suffered from headaches during the past week.

General Appearance. The patient is a well-developed adult male, very apathetic and in a semi-stuporous state. He cannot answer questions intelligently but does respond when spoken to. His response consists usually of grunts, but occasionally he gives an incoherent answer. While being spoken to he uses the right arm continuously, takes the comb out of the interpreter's jacket and puts it to his head and tries to comb his hair and then returns it to the owner. When given a hand mirror with its back toward him, he turns it around and looks at himself and returns it to the owner.

Pupils are equal, right slightly larger; react to light; impossible to test for accommodation and convergence, also for associated movements. Ptosis of both eyelids is present, and is more marked on the right side. When he sleeps the left eyelids are not completely closed. When he opens his mouth and shows his teeth the mouth is drawn toward the right side, and the nasolabial fold on the right side is much more prominent than that on the left side. The right corner of the mouth is also drawn up. There is no apparent weakness of the occipitofrontalis and corrugator muscles, although when he was asked to look upward this morning there was an apparent weakness of the muscles on the left side. The tongue is moist and coated and shows slight tremor and

deviates toward the left. Pulse varies in rate, at times fairly slow and then increases in rate, is full, comes up quickly and recedes quickly; tension good.

The right arm is well-developed; the power and motion are good. The left arm hangs lifeless at his side, but is not atrophied. The right leg is fairly well-developed and power is apparently good. The left leg is fairly well-developed, but power is lost; no atrophy or spasticity present. The tendon reflexes are prompt. The Babinski reflex is obtained on both sides.

He is semi-delirious; talks incoherently; he has an old perforation in attic of ear drum; no apparent evidence of neurosis; no bulging of upper back wall; chronic naso-pharyngitis; no evidence of sinus trouble obtainable; ear discharging pus. Pulse rapid, full, of high tension. Vessels of conjunctiva of right eye are injected. Temperature varied from 98.6° to 102°, and was never subnormal; pulse from 80 to 110; respiration from 20 to 25 or 30.

Autopsy. Tuberculous meningitis; miliary tuberculosis of both lungs; congestion of lungs.

Case V.— *Abscess of Left Temporal Lobe in Left-handed Person.* A case under the care of Dr. Daniel M. Hoyt, from whom the earlier notes were obtained.

The patient, a man, had had scarlet fever when a child. In 1896 he caught a severe cold and discharge from both ears began soon after this. He noticed distinct loss of weight during that winter. In 1898 he had marked swelling and pain over the frontal sinuses. He had a section of bone removed from the nose about one month ago, and had had numerous operations for removal of nasal polyps. He has a continuous mucopurulent discharge from both ears.

May 22d. He complains of chilliness; pulse is 99; temperature 101°.

23d. He has pain over the left temple and is delirious. Temperature 101°, evening 102°; pulse varies between 60 and 100. Pain over the temporosphenoidal region continues. Examination of the eye-grounds by Dr. Randall is negative.

26th. He has been more or less delirious since last note. Temperature is normal, pulse is 60. When he got up to pass urine gait was a little unsteady. Examination by nasal speculum shows pus coming from the upper portions of the nares, probably from the superior meatus. He is still in semi-stupor. The discharge from the left ear has notably lessened.

He was examined by me May 28th, and the following notes were made: He is partly stuporous and it is difficult to arouse him, but he can be aroused and replies correctly to simple questions. He recognizes me and calls me by name. He is not motor aphasic and not word-deaf. The irides respond to light. Pupillary reaction in accommodation and convergence cannot be determined because of difficulty in fixing the patient's attention. Extraocular muscles are normal. The muscular supply of each facial nerve is normal, the patient wrinkles his forehead, closes his eyelids, and draws up each corner of the mouth normally. The tongue is protruded straight and is normal. Each masseter muscle contracts well. Sensations for touch and pain are normal in the face and all the limbs.

The movements of the upper limbs are normal. The grasp of the hands is fair and equal on the two sides. The finger to the nose test shows no ataxia on either side.

The movements of the lower limbs are free at all parts. The patellar reflex is present on each side and probably diminished. He has no ankle clonus and no rigidity of the limbs. Sensitiveness of the sole of each foot is excessive, and therefore it is impossible to determine the presence of a Babinski reflex. Heel to knee test is fairly well performed on each side. He is not made to stand up as his condition does not permit the test. There are no localizing signs, and although the patient is not word-deaf he is left-handed, as is his child also, although he writes with his right hand.

Dr. Randall, thinking the source of infection might be in the nasal sinuses, following this examination, cleaned out the sphenoidal and ethmoidal cells, but found very little pus in these cavities. Pain over the left temporal region continues.

I examined him again May 29th and found that the stupor had increased and that he was no longer able to pay attention to what was said to him, and that it was impossible to arouse him. Babinski's reflex was now distinct and typical on both sides.

Dr. C. H. Frazier operated on May 29th. When the dura was opened a portion of the temporosphenoidal lobe protruded, showing considerable pressure. The handle of the knife was introduced between the dura and the brain toward the base of the skull, and at once a gush of flocculent cerebrospinal fluid occurred. The evacuation of this fluid at once relieved the excessive pressure and the brain collapsed within the opening. On further examination an abscess was found in the temporosphenoidal lobe, containing possibly 3 to 4 drams of pus. The pus was evacuated and the cavity in the base of the brain thoroughly irrigated. Leukocytes on June 4th were 19,040. He died June 6th.

The necropsy was performed in the presence of Dr. Hoyt, and from him I have obtained the following notes: From the trephine opening in the temporal region was found protruding an intermixture of blood clot and broken-down brain substance. Two stitches still remained in the upper angle of the wound in the dura. On removing the skull-cap the dura was found slightly adherent to the skull, its appearance opaque, not thickened, veins markedly congested and dilated, containing clotted blood and injecting fluid. Before removing the brain there was noted on the lateral surface of

the left frontal lobe a collection of pus without apparently any marked destruction of the brain substance beneath, and apparently of recent formation. On removing the brain the dura was found exceedingly adherent upon the left side, especially in the middle fossa. The left temporosphenoidal lobe was found to be exceedingly soft throughout, and in its centre was an abscess cavity containing quantities of necrotic material, but from superficial examination no fresh pus. It was impossible to trace any direct communication between the collection of pus on the left frontal lobe and the cavity in the temporosphenoidal lobe. Spreading over the base of the brain around the vessels of the circle of Willis, the pons and both lobes of the cerebellum, was a collection of yellowish white pus with apparently some distruction of the brain substance at the base. This purulent material extended down into the spinal canal as far as could be seen through the foramen magnum. On an examination of the base of the skull the following facts were determined:

Over the frontal sinuses the bone was apparently perfectly normal. There were no sinuses leading into the sphenoidal or ethmoidal cells. The sphenoidal cells on both sides were inspected; they both contained a small amount of gelatinous material, the right more than the left. The walls of these cells appeared normal. Upon the anterior portion of the petrous portion of the left temporal bone were found several openings, from one of which, the largest, when it was opened further, pus exuded. These openings communicated with the tympanic cavity.

METT'S METHOD FOR ESTIMATING THE ACTIVITY OF PEPSIN.[1]

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While the methods for the estimation of the total acidity, free acid, etc., in the gastric contents have long been sufficiently perfected for satisfactory clinical use, the same cannot be said of the quantitative methods of estimating pepsin. The belief current among most stomach specialists that pepsin is rarely at fault, and then only when the hydrochloric acid is much reduced or absent, has discouraged activity in this direction. Nierenstein and Schiff (*Arch. f. Verdauungskrank.*, vol. viii, 1902) and others have shown, however, that "diluting secretion, pepsin secretion, and hydrochloric acid secretion are to be regarded as three distinct expressions of the secretory activity of the glandular parenchyma."

Within recent years two promising methods for the clinical estimation of pepsin have come into prominence, those of Hammerschlag and Mett. The former has been widely tried, but on the whole has not been very favorably received. One of us has used it rather extensively with considerable satisfaction, but now prefers the Mett method, as it is simpler and more accurate. The Hammerschlag method (*Intern. klinische Rundschau*, 1894) is open to all the objections raised against the Esbach method of estimating albumen, as well as to others, which it shares in common with Mett's and other pepsin methods. A review of the literature of Hammerschlag's method may be found in the article by Robin in the *Arch. f. Verdauungskrank.*, 1904.

Mett's method (*Contribution à l'Inervation de la Glande sous Stomacale*, St. Petersburg, 1889) has been employed in Pawlow's laboratory in St. Petersburg since 1889, but was introduced into clinical use by Linoissier (*Journ. de Physiol. et de Path. générale*, 1889) ten years later, or five years after Hammerschlag's method was published. Mett's original article is not accessible, except in Russian, but a good description of the method is found in Pawlow's *Work of the Digestive Glands*, London, 1902, p. 25, from which we quote:

"It consists in this: Fluid egg-white is sucked up into a fine glass tube of 1 to 2 mm. lumen and coagulated therein at a definite temperature (95° C.). The tube is then cut into small pieces, which are placed in 1 or 2 c.c. of the fluid to be investigated. The whole is kept in the thermostat at 37° C., and requires no further watching. Solution of the proteid occurs at the ends of the small glass tubes. After the termination of a certain period (ten hours) the lengths of the pieces of tube and of the undigested ends of the proteid column are measured off with the aid of a millimeter scale and a microscope of low magnifying power. The difference gives the length of the digested proteid cylinders in millimeters and fractions of millimeters."

Experiments in the Pawlow laboratory by Samojloff showed that the "digestion of the proteid columns" was "directly proportional to the length of the period of digestion."

Other researches by Borrisow established the rule that

[1] Read before the Pathological Society of Philadelphia, June 14, 1906.

"the quantity of pepsin in the compared fluids is proportional to the square of the rapidity of digestion, *i. e.*, to the square of the column (expressed in millimeters) which the juices are capable of digesting in the same period of time." Schuetz (*Zeits. f. Physiol. Chemie*, 1885, p. 577) had previously established this law for peptic activity by other methods. As Samojloff (*Archiv. des Sciences Biol.*, St. Petersburg, 1893, tome ii) has shown, this is not true even for pure gastric juice in concentrated solution. It is still less true for concentrated chyme.

We will not attempt to describe all the modifications in technique that have been proposed by the numerous workers who have employed this method, though we have availed ourselves of such as proved useful. It will be necessary to refer to the work of Linoissier (*loc. cit.*) and of Nierenstein and Schiff (*loc. cit.*), since they introduced modifications in the test which are essential to adapt it to clinical use. The French writer described a method embodying the necessary changes, but it was left to the German authors to simplify and popularize these alterations. The latter consist, first, in a dilution of the stomach contents with a weak HCl solution to overcome the inhibition present in the concentrated chyme, to equalize the acidity, and to prevent too great a depth of digestion; and second, in a corresponding prolongation of the period of digestion. Nierenstein and Schiff attribute the low results found in concentrated chyme, to inhibition due to digested products (particularly carbohydrates) in solution. That this cannot be the sole reason is shown by Samojloff's work with pure gastric juice, quoted above. Danilewski and others have adduced evidence of a specific antipepsin. We will now describe the technique of the test somewhat minutely.

For filling the tubes we employ the whites of two or three eggs, well mixed to render the fluid as homogeneous as possible. Onuf (*Journal of the American Medical Association*, February 10, 1906) dries and re-dissolves the egg-albumen, but this does not seem necessary to us, as we have been struck with the uniform results obtained with different lots of albumen. Thick-walled tubes of a calibre of 1 to 1.5 mm. are preferable to those of thinner walls and larger calibre, as they fracture more accurately, and yield more uniform albumen columns. Sections of tubing, suited in length to the vessel to be employed in boiling, are filled with fluid egg-white by suction, and plugged with little balls of bread. When a sufficient number of tubes has been prepared they are dropped into a pan containing warm water, which is rapidly brought to the boiling point. This temperature should be maintained for five minutes. Violent ebullition is to be avoided as it may cause the formation of bubbles in the albumen, or expel the latter altogether. The use of the boiling temperature simplifies the test without greatly impairing its accuracy (Sahli, *Diagnosis*, Philadelphia, 1905). After drying, the tubes are hermetically sealed with sealing wax or paraffin, and allowed to ripen for several days. Fine bubbles, which are seen at first, gradually disappear, and the tubes remain in good condition for a long time, being practically sterile. When needed for use these tube lengths are cut into sections, 2 to 3 centimeters in length, with a triangular file; accurate fraction of both glass and egg-white is the rule. Portions showing retraction of the albumen or bubbles are rejected.

For ordinary routine estimations we employ the undiluted gastric contents (15 c.c. or less) a dilution of one-fourth 4 c.c. to 12 c.c.) and a dilution of one-sixteenth (1 c.c. of contents to 15 c.c. of one-twentieth normal HCl). The latter dilution is the one used for quantitative comparisons. Two Mett's tubes are placed in each dish, covered Stender dishes are most convenient, and the specimens allowed to digest in the incubator (37° C.) for twenty-four hours. At the end of this period the digested cylinders of egg-albumen at each of the four ends are measured off, and the average reading calculated for each specimen. The relative amount of pepsin is then obtained by squaring the result, and if desired, multiplying by the dilution, *e. g.*, by 16. By using Cowie's table of squares (*Physician and Surgeon*, vol. xxvi, 1904) even this mild mathematical exercise may be avoided. For making the measurements a pair of calipers with a vernier reading 0.1 of a mm. is very convenient. A lens is useful principally for reading the vernier. One end of the tube is placed against one jaw of the instrument, and then the other jaw is separated until its edge is just visible through the opalescent edge of the albumen. If the tube is at all oblique the shortest side is taken, while if the albumen is uneven the highest point to which digestion has reached is measured. Air bubbles or separation of the albumen may lead to diminished or increased digestion, but the cause is usually evident.

To ascertain to what extent slight variations in the technique, such as are unavoidable in the ordinary clinical laboratory, affect the results of the test, we made several series of estimations, varying the conditions of the experiment in each case.

1. *Differences in the Caliber of the Tubes.* Pawlow states "that the diameter of the tube, even within wide limits, is without importance." Our tubes, with the exception noted below, were all within the usual limits, 1 to 2 mm. In the following series of twenty estimations a relatively large and a relatively narrow tube were placed in each test mixture. As will be seen by the table the differences between opposite ends of the same tube are equally as great as between tubes of different caliber. The greatest difference between any two readings was 0.6 mm.; the greatest difference between any reading and the average of four readings was only 0.4 mm. This demonstrates not only the unimportance of

the exact size of the tubes, but also the accuracy of the readings in any given case.

TABLE I.

	Large caliber tube.		*Small caliber tube.*		
No.	Max.	Min.	Max.	Min.	Average.
1.	8.2 mm.	3.0 mm.	3.2 mm.	3.2 mm.	3.28
2.	2.8 "	2.8 "	2.8 "	2.8 "	2.8
3.	1.4 "	1.3 "	1.6 "	1.5 "	1.5
4.	2.4 "	2.4 "	3.0 "	2.4 "	2.6
5.	3.0 "	2.4 "	2.9 "	2.6 "	2.7
6.	2.1 "	1.9 "	1.9 "	1.9 "	2.0
7.	2.7 "	2.5 "	2.2 "	2.5 "	2.5
8.	2.7 "	2.7 "	2.7 "	2.5 "	2.7
9.	2.9 "	2.9 "	3.0 "	2.9 "	2.9
10.	8.0 "	2.8 "	2.8 "	2.7 "	2.8
11.	3.3 "	3.2 "	3.3 "	3.1 "	3.2
12.	1.0 "	0.9 "	0.8 "	0.8 "	0.9
13.	1.0 "	1.0 "	1.4 "	1.2 "	1.2
14.	1.2 "	1.1 "	1.4 "	1.2 "	1.2
15.	1.4 "	1.3 "	1.4 "	1.0 "	1.3
16.	1.3 "	1.3 "	1.7 "	1.6 "	1.5
17.	8.5 "	3.4 "	3.5 "	3.3 "	3.4
18.	2.0 "	1.9 "	2.0 "	1.9 "	2.0
19.	2.0 "	1.8 "	2.0 "	1.9 "	1.9
20.	1.0 "	1.1 "	1.0 "	1.0 "	1.1

In a second series of tests the caliber of the larger tubes exceeded 2 mm. In each case there seems to have been uniformly greater digestion in the large caliber tubes.

TABLE II.

	Large caliber tube.		*Small caliber tube.*		
No.	Max.	Min.	Max.	Min.	Average.
21.	4.7 mm.	4.5 mm.	3.3 mm.	3.3 mm.	
22.	3.4 "	3.1 "	2.4 "	2.3 "	
23.	2.5 "	2.5 "	1.7 "	1.8 "	
24.	2.4 "	2.4 "	2.0 "	2.0 "	

2. *The Age of the Tubes.* Provided there is no separation of the albumen, nor putrefactive softening, age does not seem to affect the tubes. The method of preparation tends to make them sterile. Tubes that are too fresh (less than three or four days old) are said to digest more rapidly than those that are "ripe."

TABLE III.—Table of tests to determine the effect of age on degree of the digestive tubes. Mett tubes, varying in age from five months to four days; 0.5% pepsin solution in 1/20 normal HCl. solution. Time, thirteen hours.

No.	Average.	No. tubes.	Readings.	Remarks.
1 (oldest).	6.5 mm.	3	6	Five months old.
2.	5.3 "	4	8	Several months old.
3.	6.4 "	3	6	Several weeks old.
4.	8.5 "	1	2	Nos. 4 to 6, four days old.
5.	6.3 "	3	6	Same heated for longer period.
6.	6. "	2	4	Prepared as No. 5; different egg.

It will be noted that in four of the six tests in the last table, including tubes varying in age from five months to four days, the results were quite uniform. In test four another factor enters in, for in this case a lower degree of heat (80°) was used for coagulating the albumen, evidently insufficient. In five and six the heat was also low, but was continued for ten minutes. This shows that the degree of heat and its duration is important. Owing to the difficulty of keeping the temperature at 90° as originally recommended it is better always to boil for five minutes.

The following table, adapted from Linoissier, shows the effect of variations in the time and temperature used for coagulation:

TABLE IV.

Temperature.	Time.	Digestion.
80° C.	1 minute.	17.40 mm.
" "	5 "	15.75 "
90° "	1 "	12.75 "
" "	5 "	10.30 "
100° "	1 "	11.10 "
" "	5 "	10.00 "

3. *Variations in Digestibility of Albumen from Different Eggs.* This is unimportant, as Table III incidentally shows.

4. *Variations in the Time of Digestion.* The degree of digestion, within certain limits, is said to vary directly with the time of digestion. Pawlow stated this to be true for ten hours. Nierenstein and Schiff, in diluted contents, found it true for twenty-four hours. So also have Linoissier, Cowie, and others. We believe this to be true, though the only series of tests we made did not support this view. In the series of eight tests, shown in Table V, the tubes were read at thirteen and twenty-one hours. In each case the second reading was less than it theoretically should have been. As our incubator was rather erratic in its temperature, we cannot reverse previous results on the strength of this experiment.

TABLE V.—Average Readings.

No.	13 hours.	21 hours.	Theoretical.
1.	6.5	7.4	9.8
2.	5.3	5.8	7.8
3.	6.4	7.5	9.6
4.	8.5	9.5	12.7
5.	6.3	6.7	9.4
6.	6.0	6.2	9.0
7.	7.1	7.5	10.6
8.	6.3	6.6	9.4

(Eight other tests showed similar results.)

5. *Variations in the Temperature of the Incubator.* This is undoubtedly of importance, but we have no data to offer.

The effect of variations in the original acidity of the gastric contents has been provided against in the technique of the method. The effect of inhibitory factors was studied by Nierenstein and Schiff. Our experiments in this line are described in detail elsewhere.

On the whole, therefore, we have in Mett's method, as modified by Nierenstein and Schiff, a sufficiently accurate measure of the activity of pepsin. Owing to the nature of pepsin, and the complex character of the inhibitory factors, very exact comparative estimations are not to be expected. With careful technique, however, the test is found to be surprisingly accurate in any given case. When the inhibitory factors are better understood it will be still more available, and itself offers the best means of unraveling the tangle. As a qualitative or roughly a quantitative method it also has much to recommend it, since the tubes are easy to prepare, and may be more readily preserved than the customary discs of egg albumen. We have made between 400 and 500 tests, partly experimental and partly clinical, and are well satisfied with the results, some of which will be published shortly.

B. J. C.

A CASE OF ANEURYSM OF THE ARCH OF THE AORTA PRODUCING A BRONCHO-ŒSOPHAGEAL FISTULA.

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(From the Department of Clinical Medicine, service of Professor Musser, and the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst foundation.)

The case that we report herewith is interesting in view of its remarkable clinical manifestations and the unusual pathological findings which serve to explain the sequence of the clinical events. It occurred in the University Hospital in the service of Dr. Musser, to whom we are indebted for the use of the clinical data.

The clinical history of the case is as follows: The patient, a woman, aged thirty-seven years, and a native of Ireland, was admitted to the hospital, November 13, 1905. She came to this country twenty-two years ago. Her family history presents no features bearing any relation to her condition. She was married at twenty-three, has had no children, and claims to have had no miscarriages. No history of specific infection is obtainable in herself or her husband.

Previous Medical History. The patient had measles, whooping-cough, scarlet fever, and chicken pox in childhood. There is also a doubtful history of diphtheria. Menstruation began at twelve years, was regular, painless, and lasted from three days to a week, until after she was married. After having been married several years she began to have dysmenorrhœa and the flow became prolonged at each period until finally she had a continuous flow and pain for nearly two years. She was operated on about four years ago at the Pennsylvania Hospital, the uterus being removed, she says, because of a tumor. She was perfectly well otherwise until January, 1905, when she had some cardiac trouble, manifesting itself by œdema, dyspnœa, palpitation of the heart, and precordial pain, increased upon exertion. At this time she had also a severe cough occurring in paroxysms that lasted at times an hour. These symptoms passed away and she felt perfectly well and was able to perform her own housework until the present illness began.

History of the Present Illness. About two and one-half months ago, without any known cause, the patient began to have pain in the right side of the chest. This pain was worse on exertion and was especially aggravated by using the right arm It was at times relieved by lying down, but grew progressively worse. About six weeks ago her sister looked at her chest and noticed a lump, which, as she expresses it, "jumped up and down." From that time on the patient herself has been aware of the "beating" of this lump. For the past month the patient has suffered excruciating pain and has at times been unable to sleep during an entire night. This prominence has been growing progressively more tender and she is troubled with some dyspnœa, palpitation, and a little cough, and she says her voice is becoming husky.

Physical Examination by Dr. Kelly. The patient is a fairly well-developed female subject with good bony development, fair musculature, and slight panniculus adiposus. There is no œdema, no cyanosis, no jaundice, no pallor of the visible mucous membranes and no noteworthy enlargement of the superficial lymphatics. The chest is of good length, good anteroposterior diameter, and symmetrical, except for the bulging presently to be noted. The inspiratory expansion of the chest is slight, less on the left side than on the right.

Normal pulmonary resonance extends to the sixth rib anteriorly in the midclavicular line; at the left edge of the sternum to the third interspace, and posteriorly to the eleventh dorsal spine on both sides; all move downward slightly on deep inspiration. The note in the interscapular spaces on both sides from the third to the seventh spines is somewhat impaired. The respiratory murmur throughout both lungs is vesicular in character, but throughout the whole left lung it is very faint, especially at the apex anteriorly.

The apex beat is visible and palpable in the fifth interspace, almost in the anterior axillary line; it is strong and somewhat heaving in character. To the right of the sternum from the first to the third interspace there is a globular bulging of the chest reaching forward about 1.5 cm. It exhibits a pulsation distinctly expansible in character; and over it a systolic thrill, a diastolic thrill, and a distinct diastolic shock are palpable. The superficial cardiac dulness extends upward to the upper border of the third rib, where

it joins the sternum; to the left as far as apex-beat; and to the right, a half inch to the right of the sternum. The right border of dulness continues upward along the right sternal border to the third rib, then curves outward and reaches two inches from the sternum at the second rib; it then curves upward to the top of the sternum, and finally descends along the left edge of the sternum to the third rib. The deep dulness reaches upward to the second rib; to the left as far as the apex beat; to the right one and one-quarter inches to the right of the sternum. Over the bulging a rough blowing systolic murmur and a less loud diastolic murmur are quite audible. The systolic murmur is more circumscribed to the middle and lower portions of the bulging. The second aortic sound is markedly accentuated, and the diastolic murmur sometimes seems to follow it, but apparently is not transmitted down the sternum or toward the apex. At the apex there is a soft, long, blowing, systolic murmur. The pulse in the right carotid and right radial arteries is much less marked than in the left. The liver dulness reaches to the margin of the ribs in the nipple line; the organ is indistinctly palpable.

The left pupil is slightly larger than the right; rough measurement puts the left pupil at 5 mm., the right at 3 mm.; both react well to light and accommodation. There is no change in the color of the two sides of the face, and no unilateral sweating.

Urine Analysis: November 14th: Pale, almost colorless; clear; heavy, white precipitate; faintly alkaline; specific gravity, 1018; no albumin; no sugar. Microscope shows many ammonio-magnesium-phosphate crystals.

Examination of the Blood Revealed: Hæmoglobin, 80 per cent.; red blood corpuscles, 4,340,000; white blood corpuscles, 8800.

The following notes indicate the progress of the patient's condition:

November 14th. The patient is suffering severe pain at the seat of the aneurysm and is comfortable only when kept propped up and leaning forward.

19th. Pain is complained of at the site of the bulging and along the vertebral border of the right scapula.

23d. The patient to-day experiences some difficulty in swallowing, and complains of a lump rising in her throat when she tries to swallow.

24th. The difficulty in deglutition is much more marked and the patient cannot swallow solid food. She has more cough to-day and some difficulty in breathing. She is unable to lie down. Pain persists in the back, in the precordium, and over the bulging.

25th. The prominence to the right of the sternum previously noted has markedly subsided, being now elevated scarcely above the general level of the chest. The palpatory signs remain unchanged. Posteriorly the right side seems considerably more prominent than the left. The point of maximum bulging is in the interscapular space near the spine. Over the interscapular space on the right side there is marked dulness from the third to the eighth rib. Below, there is a narrow area of resonance. Over this dull area, breath sounds and fremitus are absent; there is no palpable pulsation.

30th. There has been no material change in the patient's condition. Examination of the eye-grounds by Dr. de Schweinitz shows the retinal arteries presenting a marked expansile pulsation, similar to that in aneurysm of the aortic arch.

December 6th. Condition is little changed. The patient eats almost nothing, due to the increasing difficulty in swallowing. She is rapidly losing weight and strength.

9th. The bulging in the right of the sternum has not only greatly subsided, but the expansile pulsation is no longer visible and the palpatory signs have largely diminished, the systolic thrill alone being distinctly felt. The auscultatory signs remain unchanged, but the murmurs are not so loud as they were. The difficulty in deglutition becomes progressively greater, and the patient has a much more persistent hard cough with considerable expectoration of thick gray clumps of mucus.

11th. The difficulty in deglutition has become more marked during the past twenty-four hours. She can swallow practically nothing without having a severe paroxysm of coughing, so that it is necessary to resort to rectal feeding, and to the giving of water by the bowel to relieve thirst. To-day the patient coughs a great deal and at times the breathing is harsh and noisy, as though the bronchi were compressed.

14th. Dyspnœa and cough are more marked; otherwise the condition is unchanged.

15th. This morning the patient's condition is much worse than at any time since she has been in the hospital. She is markedly cyanosed, her lips and finger-nails being a distinct blue; she is very dyspnœic and loud bronchial rales can be heard some feet away from the bed. She can no longer swallow and complains of pain over the entire chest and back. Her mind is not perfectly clear.

15th, 11 A.M. The patient suddenly became extremely cyanosed, her face grew purple, and she fell over dead.

From the time of admission the temperature, pulse, and respiration presented no markedly abnormal features, except an occasional rise in the respiratory rate, until November 29th, when the respirations rose to between 24 and 28 in the minute, and remained so until December 5th, when they increased to between 32 and 40, ascending at one time to 42. At about the same time variations in the temperature were noted, and the fluctuations varied between 98° and 102° from then until death. The pulse-rate remained

between 80 and 100 throughout the patient's stay in the hospital.

With these clinical data at hand little hesitancy would be entertained in making a diagnosis of aneurysm of the arch of the aorta. The particularly interesting features to determine were the cause of the disappearance of the pulsating tumor in the upper thorax anteriorly, the coincident onset of dyspnœa and dysphagia, and the cause of the patient's sudden death with symptoms of asphyxia. It is in regard to these questions that interesting findings were contributed by the postmortem examination, from the notes of which we have extracted the following:

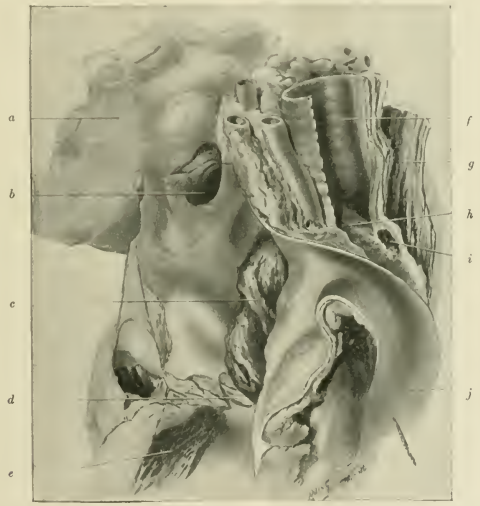

FIG. 1.—Gross appearance of the aneurysm and adjacent organs, to show the broncho-œsophageal fistula: *a*, sternum; *b*, anterior aneurysm; *c*, posterior aneurysm; *d*, aortic valve; *e*, left ventricular wall; *f*, trachea; *g*, œsophagus; *h*, bulging due to aneurysm; *i*, fistula between left bronchus and œsophagus; *j*, aorta.

The only features of any pathological interest in the organs of the abdominal cavity were a moderate degree of chronic passive congestion of the liver, spleen, and kidneys.

The organs of the thoracic cavity presented in brief the following findings: As the sternum was removed there was found to be adherent to it, at the junction of the second costal cartilage with the sternum, an aneurysm arising from the junction of approximately the ascending and the transverse portions of the arch of the aorta (Fig. 1). Its main axis was anteriorly in the direction of its attachment to the sternum. It contained a grayish-red laminated clot which projected into the left ventricle, where it was attached to the musculi pectinati.

On the posterior wall of the ascending arch and considerably nearer to the aortic leaflets than the preceding aneurysm, was a second aneurysm, which, extending posteriorly, compressed the trachea at the level of the bifurcation. The aneurysm had broken down the arch of the tracheal rings and had exerted such pressure on the posterior wall as to produce necrosis with a resulting fistula between the left bronchus just below the bifurcation and the œsophagus. This perforation was approximately 0.5 cm. in diameter, its edges necrotic and foul smelling. As the trachea was incised considerably above the level of the fistula, it was found filled with a milky substance presenting throughout the characteristics of ingested liquid food. The mucous membrane of the trachea was intensely congested. The bronchi were partially filled with a liquid having the characteristics of that described in the trachea. With the slightest pressure exerted on the lungs this fluid welled up in the bronchi. The lungs presented throughout all five lobes a partial consolidation. On section numerous grayish-white prominences were noted, giving the tissues an extremely granular appearance. These areas were especially numerous

in the lower right lobe, where, by their confluence, the lung assumed a practically solid appearance.

Histological Examination. Sections were prepared and studied from all the organs, but only that of the lung has any bearing upon the interesting features of the case. This section shows areas in which the tissue is practically free from pathological lesions and adjoining them and scattered through them, areas in which the alveoli are filled with an exudate composed primarily of polynuclear and mononuclear cells and a few epithelial elements. There is a moderate amount of œdema and many alveoli contain a granular material apparently of extraneous origin. The peribronchial vessels are intensely congested and in the submucous layers a moderate round-cell infiltration is seen.

Our interpretation of the pathological findings as bearing on the clinical features of the case are as follows: When the patient entered the hospital there existed the aneurysm which presented anteriorly and became adherent to the sternum, and in all probability the one of smaller dimensions arising from the posterior wall of the ascending arch. Later the wall of this aneurysm weakening permitted its increase in size, thus compressing the trachea and œsophagus and producing the consequent dyspnœa and dysphagia. Furthermore as this aneurysm was situated nearer to the left ventricle than the one located anteriorly, it received the force of each systole and thus permitted the subsidence of the signs associated with the aneurysm presenting anteriorly. This was apparently the existing state until about December 5th, when the rise in respiratory rate occurred, and was followed within a few days by the beginning of rather marked temperature fluctuations and the clinical observation that the patient had a much more persistent cough than previously, and associated with it considerable expectoration. It was at this time that a slight perforation in all probability occurred between the œsophagus and trachea, sufficient to produce an aspiration pneumonia. These conditions existed until just prior to death, when the fistula suddenly becoming enlarged, permitted the flooding of the respiratory tract by the ingested fluids, which had been prevented from passing into the stomach by the obstruction of the œsophagus from the aneurysm.

Œsophageal fistulæ may be divided primarily into two general classes, congenital and acquired.

Congenital œsophageal fistulæ, according to the exhaustive analysis of congenital anomalies of the œsophagus by Kraus,[1] are of one of two types: (1) Simple tracheo-œsophageal fistulæ. In this type there is a simple communication between the œsophagus and the trachea at the point of bifurcation of the latter. The position of the fistula at this point is determined by the fact that here the closure between the respiratory passages and the gut tract, from which the former develops, occurs latest. (2) The more common type of congenital œsophageal fistulæ is associated with imperforate œsophagus. The upper portion of the œsophagus is usually more or less dilated, ending abruptly at the level of bifurcation of the trachea, just above which occurs a communication between the œsophagus and the trachea.

Acquired œsophageal fistulæ may be primary or secondary. Primary fistulæ are those resulting from diseases of the œsophagus itself. Secondary fistulæ are those consequent upon diseases of neighboring parts which involve the œsophagus by extension or cause sufficient pressure to induce necrosis and consequent perforation. In general, primary and secondary perforations have occurred with almost equal frequency, the slight inequality being in favor of the primary. Of twenty-four cases observed by Zenker[2] twelve were primary, nine secondary, and three doubtful. However, when we consider perforations from the œsophagus into the air passages alone we find primary perforations greatly preponderating, the secondary almost a rarity. As to sex, œsophageal fistulæ are much more frequent in males than in females. Of Zenker's twenty-four cases, nineteen occurred in males, and in an analysis of one hundred and fourteen cases by Zenker and Ziemssen, seventy-seven were in male subjects, twenty-five in female, while in twelve the sex was unknown. Of Vigla's[3] eighteen cases, fourteen were in males. In regard to age, the greatest number appear to occur between the ages of forty and fifty. As to the frequency of the various causes of primary perforation,* leading to fistula between the œsophagus and the neighboring parts, carcinoma of the œsophagus is usually looked upon as the most common, an opinion seemingly warranted by the fact that of sixty-four reported cases of primary perforations, thirty-eight were the result of œsophageal carcinoma. Zenker and Ziemssen, in a very careful analysis, look upon the apparent frequency of carcinoma as a cause of perforation as false, claiming that on account of the more striking clinical picture and the greater severity of symptoms in carcinoma of the œsophagus, as compared with the other causes of perforation, these cases are more commonly reported in the literature. They hold that the true proportions are more accurately expressed by the twelve cases of their own observation, in which eight were due to traction diverticulæ, two to carcinoma, and two to ulcerations of a non-carcinomatous nature.

As regards secondary perforations, amongst the various causes are abscesses and softening of either tuberculous or anthracotic tracheal or bronchial lymph glands; abscess of the mediastinum or the retropharyngeal tissue, resulting from tuberculosis of the cervical or upper dorsal vertebræ; ulcerations of various origin of the trachea, amongst which

* Cases of sudden perforation in a previously healthy œsophagus, classed as ruptures, an exhaustive analysis of which will be found by McWeeney (Lancet, July 21, 1900), are not considered in this paper.

those of syphilitic and carcinomatous origin are the most prominent; gangrene of the lung; finally, pressure on the œsophagus from without, amongst the causes of which may be mentioned aneurysm, goitre, and the various tumors of the neck.

To consider the various organs and parts with which œsophageal fistulæ may communicate, Zenker and Ziemssen in an analysis of one hundred and seventeen cases, found the communication to have occurred in the following frequency with the organs mentioned:

Right bronchus	14	
Left bronchus	12	= 26
Trachea	21	
Right lung	17	
Left lung	6	
Right pleural cavity	10	
Left pleural cavity	1	
Pericardium	7	
Left auricle	1	
Aorta	18	
Pulmonary artery	1	
Carotid artery	1	
Subclavian artery	2	
Inferior thyroid artery	1	
Intercostal artery	1	
Vena cava	1	
Azygos vein	1	
Cyst of thyroid	2	

In the above tabulated cases, practically 60 per cent. of the perforations were between the œsophagus and some portion of the air passages, and 22 per cent. occurred between the œsophagus and one of the bronchi.

A brief reference to the more prominent features of our case shows it to belong to the type of secondary fistulæ. Though perforation between the œsophagus and bronchus is one of the relatively frequent forms the case is unique by reason of its cause. In the literature on the subject we are able to find but one similar case, that reported by Habershon:[4] The patient, a man of twenty-three years, gave a history of a traumatic aneurysm of the ascending arch of the aorta which produced death by perforating into the pericardium. For a week preceding death he had experienced considerable difficulty in deglutition, and at the autopsy, pressure necrosis and a resulting fistula were found between the œsophagus and the left bronchus just below the point of bifurcation. The rupture of the aneurysm was not at this point. It is an interesting fact that the position of the fistula in this case corresponds exactly with that in ours.

Amongst the numerous cases of fistula between the œsophagus and the air passages of various origin reported are some with most bizarre features. Aufrecht[5] reports a case in which there was a fistula in the suprasternal notch from the larynx to the external surface, and 2 cm. below the level of the suprasternal notch was another between the bronchus and the œsophagus, so that a great portion of the liquids swallowed reappeared at the suprasternal notch. Cartier and Masson[6] report a case of tracheo-œsophageal fistula resulting from a cannula left in the trachea for six years after a tracheotomy.

In the diagnosis of broncho-œsophageal or tracheo-œsophageal fistula, naturally the pathological condition producing the fistula must receive due consideration. An almost constant feature is, moreover, laryngitis and cough consequent upon it and upon irritations of the laryngeal mucous membrane by food particles. Later, almost invariably, aspiration pneumonia develops and is usually a forerunner of death, though abscess or gangrene of the lung may develop before death relieves the patient of a miserable existence.

There are many phenomena that may be observed to lend evidence to the diagnosis of fistula between the œsophagus and the air passages. Kohlenberger,[7] in an article on tracheo-œsophageal fistula, states that if after a smooth act of swallowing, in which the larynx is not irritated, food is coughed up the diagnosis is certain. Martius[8] administers fuchsin-colored bouillon and watches for its reappearance. In a patient of his own, on whom he used this test, there was perfect quiet for two minutes after the swallowing, during which time the patient rinsed his mouth well, and then coughing commenced, lasting for six minutes, during which time most of the ingested colored liquid was expelled.

Attempts have been made to apply to the diagnosis of communications between the œsophagus and the air passages the variations in pressure in the œsophagus during respiration. The first observations bearing upon this subject were made by Gerhardt.[9] While an assistant in Griesinger's Clinic in Tübingen, using the Green method of injection of astringents into the air passages for the cure of bronchitis, he attempted to evolve a definite test to determine when the tube was in the bronchus. Introducing a tube into the bronchus and holding a lighted candle before the free end, the flame was drawn toward the tube in inspiration and blown away from it in expiration. The tube was then introduced into the œsophagus, and much to Gerhardt's surprise the same phenomena were observed. The undoubtedly correct explanation for these occurrences was offered by Gerhardt: that all of the hollow organs contained within the thorax are subjected to a negative pressure during inspiration, but on account of the soft flexible walls of an organ such as the œsophagus, its upper portion acting as a valve, no air flows in from the exterior. This explanation harmonizes well with the fact that when the inner end of the tube passes beyond the boundary of the thoracic cavity, *i. e.*, into the pharynx or stomach, the movements of the flame cease.

Sixteen years later Gerhardt's assistant, Emminghaus,[10] working along the same line, attached the external end of

the tube to a water manometer to determine accurately the normal inspiratory and expiratory pressure in the œsophagus. He found that during quiet respiration the inspiratory pressure was equal to 4 cm., the expiratory pressure the same. In forced respirations the inspiratory pressure increases to 22 cm., the expiratory to 16 cm.

In 1886, Martius[11] attempted to carry the subject still farther by obtaining graphic representation of the variations in pressure in the œsophagus by means of a revolving drum. He succeeded in doing this in a very graphic way, as is shown in the accompanying diagram (Fig. 2).

The small curves superimposed on the larger ones are apparently due to the heart's action. The larger ones represent the respiratory movements. This apparatus was then used on a case of broncho-œsophageal fistula, and there was found to be almost complete obliteration of the curves

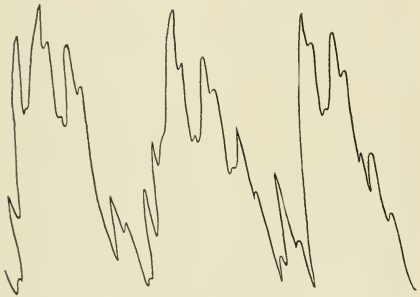

Fig. 2.—Graphic representation of variations in pressure in the œsophagus. (After Martius.)

due to the respiratory act. The cause of this may seem somewhat obscure, but it will readily be understood with the assistance of the accompanying rough diagrams (Figs. 3, 4, and 5).

Letter *A*, Fig. 3, represents the pulmonary apparatus and *B* the œsophagus; on inspiration there is negative pressure in the direction of the arrow *C*, equivalent, let us say, to ten units. If now there be a communication between the pulmonary apparatus and the œsophagus, as shown in Fig. 4, air will flow from the respiratory passages into the œsophagus in the direction of the arrow *D*, equivalent to compensate for the ten units of pressure, and perfect equilibrium will result. This, however, is subject to variations. For if the opening between the air passages and the œsophagus be small and the inspiration be powerful and quick, not sufficient air will pass through the communication to compensate for the negative pressure and there will be a balance left in favor of the latter. To express this diagrammatically, suppose that the inspiratory effort created a negative pressure in the direction of the arrow *C*, Fig. 5, equivalent to twenty units, and air was able to enter through the fistula equivalent to only ten units, there would then be ten units still in favor of the direction *C*. This series of phenomena actually occurred in Martius' patient when he was commanded to take deep inspirations, the curves reinstating themselves practically the same as in the normal cases in ordinary respirations.

Another possibility must be taken into consideration in the temporary occlusion of the fistulous opening by food or secretions and the consequent occurrence of a valve-like fistula, as in Quincke's case, in which air could enter from the bronchus into the œsophagus but could not return, in consequence of which entering the gastrointestinal tract it produced enormous meteorism.

It is thus seen that deductions in regard to intraœsophageal fistulæ must be drawn with the greatest care, at least, until

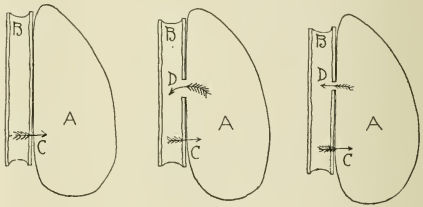

Fig. 3 Fig. 4 Fig. 5

further observations have put the subject on a more trustworthy basis.

As to the treatment of broncho-œsophageal and tracheo-œsophageal fistula, we must look to the daring advances of surgery to furnish the only possibility of a cure. The physician's attention, however, can be directed to guarding against or alleviating the complications resulting from the fistula, chief amongst which are laryngitis, bronchitis, and aspiration pneumonia.

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FLOATING KIDNEY; ITS SIGNIFICANCE AND TREATMENT, WITH SPECIAL REFERENCE TO A METHOD OF PERFORMING NEPHROPEXY.[1]

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One of the most interesting and important subjects in medicine and surgery at the present time is the significance and treatment of floating kidney.

The fact that the kidney may be abnormally mobile and displaced to a varying degree below its normal position was first observed by Rayer in 1841, that such a displacement of the organs is capable of producing symptoms was pointed out by Brochin and Oppolzer in 1864, in the same year Dietl described the symptom-complex known as Dietl's crisis, and in 1881, Hahn devised the operation of nephropexy. Further, Glénard gave us additional knowledge referable to the subject through his recognition and description of splanchnoptosis, Glénard's disease, that there may occur a more or less general ptosis of the abdominal organs.

As the study of abdominal diseases has advanced and abdominal surgery become more and more perfected, the significance of floating kidney and its treatment has received a full share of consideration. The literature upon the subject now represents at least a thousand memoirs, journal articles, and books.

The specialist in medicine and surgery recognizes the pathological influences of prolapsed kidney, and carries out, as far as scientific knowledge goes, what is believed to be a satisfactory treatment; yet the profession in general seem as yet unfamilar with its great frequency, it is often overlooked and the suffering induced by it is being widely treated as indigestion, hysteria, neurasthenia, frequently as uterine or ovarian disease, and recently often as appendicitis. On the other hand, as I shall later on point out, there exists the practice among a few physicians and surgeons to attribute every chronic illness of neurasthenic or gastrointestinal type to a movable or floating kidney, a practice deserving of the most severe criticism.

What I wish to consider with you in this presentation of the subject is the recognition of the symptoms and presence of the floating kidney causing illness, briefly the question of mechanical treatment, the surgical treatment, and particularly to place before you the results of further experience and experimentation regarding the method of performing nephropexy, first described by myself in September, 1901 (*American Medicine*, September 14 and 21, 1901).

During the last ten years I have made a careful study of a large number of cases of this with other forms of visceral ptosis, in my hospital and private practice, have in course considerable experimentation on dogs and rabbits, and although I am not prepared at this time to offer you a statistic and scientific presentation accrued from these studies, I shall place before you what is quite as important, the practical conclusions.

Floating kidney is chiefly a disease of women, not more than 1 or 2 per cent. of the cases occurring in men. Its frequency is variously estimated. Kuster, of Berlin, found that but 4.41 per cent. of the women treated in his general surgical practice had a pathologically movable kidney. Goelet and Edebohls, of New York, in their gynecological work, found 20 per cent. of the women coming to them have floating kidney, and Harris and Larrabee state that this percentage is much too low, that 50 per cent. probably have movable kidney. Still others decide that the percentage may be as high as 80. This wide range of degree of frequency, I believe, is to be explained by the varying opinions of observers as to what constitutes a floating kidney. From my experience I should say that not more than 10 per cent. of the gynecological patients coming under my care have a nephroptosis causing symptoms.

It occurs in multiparous and nulliparous women, according to the statistics we have collected from the literature in about equal proportion. The right kidney is usually the one displaced, but now and then both and sometimes the left alone.

The etiology I shall not here consider, except to state that the intrinsic cause seems to be in each case a change or diminution in the intra-abdominal pressure which maintains the abdominal viscera in position.

The patient having a floating kidney is frequently of a characteristic type: nervous, a long-waisted individual, with lax abdominal walls, is emaciated, either from exhausting disease or frequent childbearing, or more often through the associated digestive and nervous conditions from which she suffers. Some have an abundant supply of fat, and a few, those possessed of moderate good health, are well nourished.

The patient in the typical instance comes to the physician complaining of an indefinite complex of symptoms: nervousness, chronic indigestion, dragging pain in the loin, usually the right, abdominal distention, and often appendicular pain, or not rarely she has discovered a movable mass in the lumbar region. In a few, the woman will give a history of

[1] Read before the Harrisburg Academy of Medicine, March, 1906.

being taken suddenly with excruciating pain in the loin, or the physician will be called during or immediately following such an attack. The presence of nervousness, with pain in the loin and perhaps indigestion in any individual, of particularly the type referred to, should always form sufficient index for a careful study, with, if necessary, repeated physical abdominal examination, for floating kidney, gastroptosis and enteroptosis. Such patient should never, as one is wont to do, be treated symptomatically as nervous, neurasthenic, and chronic dyspeptics, to drag through months and years of miserable existence, rarely receiving the least benefit from such treatment.

Going more carefully into the symptomatology one finds that the digestive disturbances are usually chronic, manifested chiefly by persistent intestinal distention, fermentation, flatulence, and in my experience in half of the cases by a chronic mucous enterocolitis. There is gastric irritability, nausea, and sometimes vomiting. The gastric disturbance is probable in part due to pressure on the duodenum and in part reflected through the connection between the kidney and semilunar ganglion. The mucous enterocolitis, I am convinced, is here a neurosis, extending through Auerbach's or Meissner's plexus. Its presence alone I have found is an indication for an investigation of the position of the kidney. The patient complains of dragging pain in the loin, extending to the groin and into the thigh of the affected side. This, in my studies, has been the most frequent and characteristic symptom, and is directly referable to the mobile kidney changing position and being subject to insult. Championnière attributes this symptom and the gastric disturbance to direct traction on the suprarenal capsule, another recent observer to dragging and associated descent of the ascending colon.

There is in a large number of patients pain and tenderness over the appendicular region, due, according to Edebohls, to pressure of the loose kidney upon the superior mesenteric vein, with resultant venous stasis and congestion in the region of the appendix. Edebohls goes so far as to state that more or less congestion and inflammation of the vermiform appendix is present in nearly all cases of floating right kidney, and in fifty-four of seventy-four cases he found it necessary to remove the appendix with or after nephropexy. I can in no sense agree with Edebohls in this connection, believing where appendicular pain does exist it is simply coincident or is a reflex pain, a manifestation of the neurasthenia present.

The first evidence of floating kidney may be the sudden onset of an attack of severe excruciating renal pain, attended with nausea and vomiting, abdominal tenderness and a varying degree of syncope and perhaps a cessation of the flow of urine. In some the onset is less abrupt or the attack may even be gradual in its mode of onset and moderate in its manifestations. Some are relieved by posture or manual replacement of the kidney, in others the attack passes off abruptly or slowly. This symptom-complex first described by Dietl in 1864 and known as Dietl's crisis is due to kinking or obstruction of the ureter from rotation of the kidney on its short axis, or a simple angular ureteral kinking where there exists a wide range of mobility of the organ. A transient hydronephrosis often occurs from this accident. I need not point out to you that this is the most serious and important symptom and complication of a prolapsed kidney. Fortunately, it is comparatively rare, occurring in possibly 10 per cent. of the cases. Atlee saw it in three of five cases treated, and Newman in a large experience fourteen times.

Jaundice has not infrequently been observed with the condition, and by many the jaundice is thought to be caused by the mobile kidney. One writer states it was present in 15 per cent. of his cases. One can scarcely credit that jaundice is here due to other cause than coincident gallbladder, duct, or liver disease, even though it disappears after replacement of the kidney.

These women are always more or less nervous, may be extremely neurasthenic, suffering from restlessness, cardiac palpitation, insomnia, and every symptom of profound nervous exhaustion.

A careful investigation of the other abdominal organs determines in several cases an associated gastroptosis, enteroptosis, or the ptosis of the kidney forms part of a splanchnoptosis.

The severity of the symptoms, if there be symptoms, depend upon the degree of mobility of the kidney, the coincident presence of the other forms of enteroptosis, and the duration of the condition. However, many cases exist where regardless of the degree of displacement no symptoms arise. We have observed more than once a kidney displaced to the pelvic brim and the patient complaining of but slight pain in the loin or no symptoms, coming for advice simply because a tumor or mass has been discovered in the abdomen. A very large percentage of patients having a displacement of less degree are not aware of its presence until it is detected by the physician and have absolutely no symptoms.

For the determination of the presence or absence of floating kidney the physician should have considerable experience in abdominal palpation, should follow certain methods, and prepare the patient for the examination. He should remember, too, that a negative finding at one, even two sittings, does not prove that a kidney is in normal position. Even the most experienced abdominal diagnostician in a patient with rigid abdominal walls, distended intestines, with a fear of being hurt or because the kidney for the time being assumes a normal position, fails until these factors are overcome or until, I may say, a lucky examination.

He should make it the rule to make at least three examinations at intervals of a few days. It is wise, particularly in doubtful cases, to prepare the patient by having her remain in bed at home for two or three days. The bowels should be well opened each day, my preference being with a dram of Rochelle salts administered a half hour before breakfast. It is good, too, to interdict starch and saccharine foods, so that flatulence may be prevented. I think it is preferable to make the examination in bed, the abdomen being exposed from the symphysis to the sternum, the patient lying on her back with the chest elevated and thighs flexed on the abdomen. It is best to begin the examination with careful inspection and general palpation of the abdomen so as to note any prominence or mass in the lower half of the abdomen. In this way we have often detected a kidney displaced into the lower abdomen. One hand should then be placed just below the ribs and external to the rectus muscle. The other hand posteriorly, making quite strong pressure against the small triangular space below the twelfth rib. The patient should now be asked to take a long inspiration and then quickly a deep expiration. With the expiration the examiner approximates his hands, and if the kidney is movable one-half or two-thirds of it will be grasped and the organ can be made to slip away upward and backward beneath the ribs, or both hands can be approximated above the kidney, or the kidney is found in a lower position, perhaps even at the pelvic brim. The kidney must of course be differentiated from the more anterior, resisting, and less sensitive border of the liver. If the examiner fails to palpate the kidney in this way, as often happens, the patient is best placed on the side opposite to that to be palpated, the thighs flexed well on the abdomen and the lower portion of the body bent forward, and the same procedure is repeated. These two positions we have found gain the most complete relaxation of the abdominal walls and satisfactory examination. If the kidney has been palpated and has slipped upward beneath the ribs, or cannot be palpated, it can frequently be displaced downward by asking the patient to cough, or assume the erect position, take a deep inspiration and cough.

In this way the displaced kidney is found in one of two positions: First, one-half to two-thirds of it can be palpated and then the organ made to slip upward beneath the ribs. This I would designate as a movable kidney, not a true pathological condition, and rarely if ever capable of causing symptoms. Second. When the examining hands can be approximated above the kidney it can easily be displaced lower, or is found to a varying degree below this position, I would characterize as a floating kidney, which is the pathological condition capable of producing the symptoms described. In the latter condition the study of the case should not stop with the detection of the floating kidney, but a careful investigation as to the position of the stomach, inflating and outlining this organ by auscultatory percussion is to be carried out, for I have often under such circumstances found a gastroptosis likewise causing symptoms and requiring treatment. Also, one should seek to determine the presence of hepoptosis, enteroptosis, retroversion of the uterus or prolapse of an ovary, before informing the patient of the character of the illness and proceeding to the treatment of the floating kidney. I would emphasize this, because in two instances I have overlooked a gastroptosis, and after a nephropexy the patient has returned to me benefited but not cured.

Therefore, I would classify abnormal mobility of the kidney as movable kidney (non-pathogenic), floating kidney, and floating kidney with enteroptosis.

There are certain complications which are sometimes found with a floating kidney, and when present make the disease of greater significance. Albuminuria is not uncommon as a result of the disturbance of the circulation of the kidney and obstruction to the flow of urine, and it is believed nephritis may result. Abbot found a simple floating kidney not secreting urine. Southerland observed orthostatic cyclic albuminuria in fifteen cases, which always disappeared after placing the patient in bed. In 12 per cent. of Newman's cases there was hæmaturia. A transient, sometimes a permanent, hydronephrosis has resulted from the kinking of the ureter. Dietl describes several cases where the kidney was incarcerated, likewise others, and Riedel reports the remarkable experience of having found it necessary to perform cœliotomy in forty-one of one hundred and eleven cases for the purpose of relieving adhesions between the kidney and other organs.

The treatment of floating kidney is dependent upon the position of the kidney, the presence or absence of symptoms and associated complicating malposition of other abdominal organs.

It is further medical, mechanical, or surgical.

The simple movable kidney, in every instance as far as my experience has gone, is not a pathological condition, causes no symptoms, and should be completely disregarded and another cause for the illness looked for. This patient should never be told of the presence of the mobility of the kidney, and the same rule should be applied in any case of floating kidney until the physician is well satisfied that it is the kidney which is causing the ill health. It should be the first aim of the physician in every instance of displacement of the character designated as floating kidney to thoroughly study the case, and deducing from such study as accurate a conclusion as may be possible as to whether it is the kidney that is causing the symptoms. That assuming the recumbent position will many times relieve the symptoms of a prolapsed kidney is a fact to be applied in this

connection. It is not to be forgotten that indigestion, mucous enterocolitis, and pain in the right loin can as well be dependent upon other causes, and particularly that replacement of the kidney by any means will not relieve essential neurasthenia or acquired neurasthenia of other origin. To inform a patient having essential neurasthenia that she has a floating kidney, or to say to any patient that she or he has a movable kidney, is only conducive of harm and they scarcely ever fail thereafter to attribute much or all of their illness to the kidney. We know from experience that it is in these cases that the mechanical treatment does no good, and the surgical treatment often converts the patient into a miserable nervous wreck. I here want to take the opportunity to severely criticise the practice of the enthusiastic physician and surgeon, who finds a movable or floating kidney as the cause of illness in as many as 75 per cent. of the women coming to him, and accordingly applies a treatment, particularly nephropexy. In a small community, where I visited a short time ago, a physician stated to me that he had operated for floating kidney fifty times within the year, and many other physicians in this town were daily seeing cases of what was diagnosed as floating kidney. Ninety per cent. of these cases must have been a simple movable kidney and probably in some the lower border of the liver was taken for the kidney. The inference as to the amount of harm done I need not state.

In those cases where it is established that it is a floating kidney which is the cause of ill health, the symptoms are persistent and severe, the patient should be given the choice of the medical and mechanical or the surgical treatment. In the poor working woman it is best to resort at once to the operation of nephropexy. In those cases where Dietl's crisis has occurred, albuminuria or hematuria is present, or there exists a hydronephrosis the operation should be carried out without delay. Where the nephroptosis is complicated with gastroptosis, or the reverse, a general visceral ptosis is not present, and there are symptoms referable to both conditions I would strongly recommend the elevation of the stomach by plication of the gastrohepatic omentum. My experience with the operation of elevation of the stomach in eight cases has been so satisfactory as to results that I feel well warranted in stating that the combined procedures are demanded in this class of ptosis.

A retrodisplacement of the uterus should always be treated surgically with floating kidney and is often the added factor which succeeds in completely restoring the health.

The medical treatment I shall not here refer to, except to say that it consists in a modified rest treatment, if possible the complete rest treatment in bed for six weeks, with forced feeding and massage, the use of tonics, such intestinal antiseptics as hydronaphthol, regulation of the secretions, regular exercise, calisthenics following. In very rare cases with the gain of much flesh this treatment can succeed in curing the condition.

The mechanical treatment, the application of a mechanical support to the displaced kidney, is a question of considerable importance. A great many mechanical devices have been invented to support a floating kidney in position, but the large majority of them are useless, completely fail in their object, and are harmful. I shall discuss the faults of but one of them, the elastic or non-elastic abdominal binder armed with a kidney pad. In the first place the kidney pad with the patient in the erect position has not the slightest influence in maintaining the kidney in position, for it is impossible to accomplish this with the intelligent application of the hands for more than a few respirations. Also, according to the investigation of Menge such pressure is harmful. Menge found that even the pressure of the hand is not a matter of indifference. The study of the urine, after such examinations, in fifteen cases showed a previously normal urine to contain albumin and a little blood, the albumin being found in a greater quantity than could be accounted for by the amount of blood in the urine. It may be deduced from this research that the pressure of a kidney pad may be sufficient to produce nephritis or at least irritation of the kidney.

The application of a mechanical support in floating kidney, and I may say also in gastroptosis, must have for its first and practically only object the support of the abdominal walls and the increase of the intra-abdominal pressure. This is most effectually accomplished by the application of a long straight front accurately fitting corset, what is known as the modern straight front corset. It will be found that this corset makes pressure evenly and accurately upon the lower two-thirds of the abdomen, while the upper third is free. Also, that it is a firm, snugly fitting support, can be worn with comfort, and cannot get out of position. The straight front corset to be found in the shops, however, generally fails in the object described, for in the woman with a floating kidney or gastroptosis the abdomen is shallow, even scaphoid, and an accurate fit cannot be obtained. It is my custom to send such patients to a corset maker to be measured and fitted. The corset-maker, too, should appreciate the object of the corset here and have experience in making such a corset. The corset should be put on while the patient is in the recumbent position, on her back, and by a second person. It should be laced or tightened from below upward, the abdominal contents and kidney being pushed upward with the hand during the process of lacing. It should, of course, be removed at night. This I am convinced through an experience of six years is by far the most effectual and beneficial form of mechanical support, giving, when such a support can, the greatest possible relief. I have applied this method in about a third

of my cases, in some it has proved satisfactory, and others have been compelled to return for operation. This treatment, however, it is to be remembered, is never more than palliative, does not cure and in the opinion of most men who have had an extensive experience is not warrantable. Such men as Henry Morris, Edebohls, and Goelet never apply it and Treves and Aaron recommend it.

As stated in the beginning that portion of the subject to which I wish particularly to call your attention is the surgical treatment of floating kidney, the operation of nephropexy or nephrorrhaphy.

Numerous methods have been devised and described to restore the kidney in normal position and fix it there. Hahn sutured the fatty capsule to the lumbar incision; absorbable or non-absorbable sutures have been passed through the kidney fibrous capsule and parenchymatous tissue, and thence through the tissues of the quadratus lumborum muscle, with the resection of the twelfth rib, through the intercostal fibrous tissue; the fibrous capsule has been partially or completely separated and sutured to the lumbar incision; adhesions have been established to the surrounding tissue by scarification of the capsule of the kidney, by surrounding the kidney with strips of gauze or gauze packing; the so-called Garrotta's space, the retroperitoneal space in which the kidney lies, has been narrowed by suturing with catgut sutures, by removing redundant perirenal fascia and suturing the remaining edges to the muscle incision; and the method first reported by myself, whereby the kidney is secured in normal position through the action of small rubber tubes being placed around each pole of the kidney to secure adhesions, has been practised.

Without going into detail, but sufficiently for the purpose of discussion, we may say that there are five methods of performing the operation of nephropexy now in vogue: 1. The direct suture of the fibrous capsule and kidney parenchyma to the surrounding tissues. 2. The partial or complete separation of the fibrous capsule and its suture to the muscle incision, the operation of Edebohls. 3. The narrowing of the space of Garrotta by catgut suture, with suture of the perirenal fascia to the incision, the method of Harris. 4. The passing of a strip of gauze around the lower pole of the kidney to secure adhesions (Senn) or around both poles (Deaver). 5. The rubber tube method, which I shall describe later.

I will first consider with you these methods from a purely surgical standpoint.

For a number of years the method of direct suture of the capsule and cortical substance of the kidney has been widely practised. It has the fault that the sutures cut out of the kidney parenchyma and a recurrence of the condition occurs. A great many failures have resulted from this method and it has brought much discredit upon the operation of nephropexy. The fault has been, it is believed, greatly removed by the employment of the triangular suture of Brodel or Goelet, which consists of a continuous suture of silkworm-gut so introduced into the kidney structure as to describe a triangle and grasp a mass of capsule and parenchyma. Another and more serious objection to this operation is the occurrence of urinary fistula. In a review of the literature we find that five operators alone report the occurrence of thirty-seven fistula following the direct suture operation. It occurred in 10 per cent. of another's cases.

The separation of the fibrous capsule and its suture to the muscle incision (the operation of Edebohls), except that it is an extremely mutilating procedure from a purely surgical standpoint, is highly satisfactory, and I may say is the operation now usually performed. The kidney is permanently fixed somewhat below its normal position, he states, by primary union, and recurrence cannot occur. The influence of removing the capsule I shall refer to.

The passing of strips of gauze around the kidney aims to secure, first, a wide granulation surface and after a period of days, following a painful removal of the gauze, permanent perirenal adhesions. The time required here for the repair is very long, often six or eight weeks. Scar tissue with fibrous replacement of a considerable portion of the parenchyma tissue must occur in many cases, as has been found at subsequent operations, it being even necessary to perform nephrectomy, as reported by Morris. Also, such an operation is apt, from cicatricial change, to cause more pain than was present before operation, as has been experienced in some cases operated upon by Treves.

The operation devised by Harris, of Chicago, the narrowing of the space in which the kidney lies so as to constrict the range of mobility, combined with suturing the perirenal facia to the incision has the correct principle, because it is in no way mutilating. My objection to this operation is the danger of constricting the kidney structure, as it would be difficult to estimate the amount of tension which would secure the kidney and yet not press upon the structure interfering with the circulation, kinking or obstructing the ureter, and because he states that it is so often necessary to open the peritoneal cavity.

These four methods of operation, the direct suture, the Edebohls capsule splitting and suture method, the Senn-Deaver operation, and the Harris operation I have pointed out to you; all, except perhaps the Edebohls operation, have objections and these are immediate objections, purely surgical.

In addition to this, all, except the Harris operation, have the fault that in the technique at operation or following, the normal cortical, secreting structure of the kidney and the kidney fibrous capsule is more or less mutilated, and the question arises, Does the suture and cutting out of the

suture placed in the parenchyma do no harm, immediately or subsequently, does the splitting and complete removal of the fibrous capsule or the contraction of extensive granulation tissue about the kidney produce nephritis or cicatricial change in the parenchyma?

The kidneys are among the most important organs in the body, delicate in structure, have a highly specialized function, are necessary to life, and the healthy performance of their function necessary to good health. The dividing line between a healthy and diseased kidney, of nephritis and Bright's disease, is often not a broad one. As stated by Stengel at the last meeting of the American Medical Association: "This organ is subjected to exceptional irritations in its important function of excretion, and that inflammatory lesions in the minute pathological sense may be extremely frequent without of necessity having any lasting result." "That it is obvious nephritis does not become a condition of grave significance until the pathological changes have attained a certain degree of intensity, or have involved a portion of the kidney substance sufficient to interfere with the complex functions of the organ so as to imperil the health." It is a question of degree of inflammatory and degenerative disease, whether such changes take place through the presence of irritating substances in the blood or through mechanical injury or irritation from without, through surgical suture or decapsulation. Councilman, of Harvard, likewise points out from a pathological standpoint the question of degree and character, and states that in an acute interstitial nephritis not affecting the glomeruli, albumin and casts will not appear in the urine, there will be no clinical evidence of the inflammation. Still, there is the injury to the kidney substance, which, though it may not to-day influence the health, we must recognize can, under favorable conditions at least, subsequently do so. Therefore, does the surgical decapsulation of the kidney or suture of the parenchyma harmfully influence the function of the organ even though, as is generally accepted, there be no clinical evidence of it?

We have comparatively little experimental and post-mortem evidence up to the present time bearing on this question. Le Cuziat made microscopic sections of a kidney on which the suture method of nephropexy had been practised. He found a fibrous cord half a millimeter in diameter running along the entire length of each suture tract, with induration extending a distance of three to four millimeters. It seems warrantable to believe that such a fibrous cord would cut off the tubules coming from the glomeruli in the surrounding cortical substance of the kidney and place this part of the kidney out of function. The remaining portion would undergo compensatory hypertrophy, but still the kidney would be injured to a certain extent.

You are all familiar with the operation of decapsulation of the kidney practised by Edebohls for the relief of nephritis. There is much diversity of opinion regarding the value of this operation, and some experimentation has already been made to determine the truth regarding this question. It would be out of place for me to discuss this subject here. Edebohls claims as one of the arguments for the decapsulation operation in nephritis that a new capsule is formed in a period of from three weeks to three months, that sometimes it is thicker, at other times thinner than the normal, and that the new capsule simply furnishes the function of the old, doing no harm. He does not, however, prove this by personal experimentation, taking the opinion from single experimental observations. The most important evidence regarding this question has just appeared in a paper by Emerson, entitled "Studies upon the Capsule of the Kidney," *Rockefeller Institute for Medical Research*, February, 1906. *Emerson makes the following summary of the results of his work: "Evidence from various sources, based on personal observations of kidneys of various animals from five to three hundred and thirty-nine days after decapsulation of a normal kidney determines that the surgical removal of the fibrous capsule of the kidney may cause an interstitial nephritis of a greater or less extent, varying from a simple invasion of the parenchyma with connective-tissue process, in the early cases, to marked and advanced replacement fibrosis and accompanying degeneration of renal epithelium in the tubules, and occasionally, even atrophy and destruction of the glomeruli. The new capsule forms, as stated by Edebohls and others, but is four to five diameters thicker than the normal. The degeneration of the tubular epithelium and increase in connective tissue extended for a varying distance into the parenchyma, in one case half-way to the hilus."*

It would seem conclusively evinced from this experimentation that decapsulation of the kidney, as applied to the operation of nephropexy, produces the nephritis described by Emerson, and more or less interference with the function of the kidney must result, though it may not be of sufficient degree to manifest itself clinically through the finding of casts and albumin in the urine, or cause distinct ill health. It is probable that the same takes place but to a much less degree in direct suture of the kidney.

In the light of this evidence it is apparent that an operation which removes the fibrous capsule, sutures the parenchyma or in any way injures the capsule or parenchyma is unwarrantable for the relief of a simple ptosed kidney and should never be practised. Even accepting the clinical observations that no manifestation of inflammatory change follows these operations the fact still remains, is explained by the degree or extent of involvement, and may manifest itself with subsequent cause, with, for instance, an attack of one of the acute infectious diseases, as scarlet fever or

typhoid fever, or with the arteriosclerotic changes of after years. Such changes hastening the progress of the nephritis and its end.

With this knowledge the principal which to my mind is demanded in the operation of nephropexy, is that in the technique of performance of the operation neither the kidney, parenchyma, or fibrous capsule of the kidney should be injured or disturbed by suture or other means, and that no extensive pericapsulitis should follow to form tissue which will contract, press upon, or involve the underlying parenchyma. Further, the operation should avoid any cicatricial change in the lumbar incision. The adhesions to the external capsule of the kidney should be just sufficient to maintain the kidney in permanent normal position.

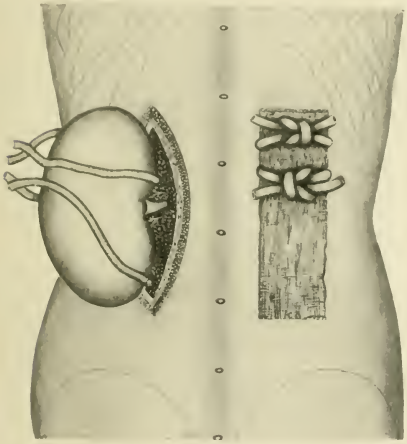

Fig. 1

Fig. 2

We believe that this principle is gained through the following operation first described by myself in *American Medicine*, September, 1901.

The operation is as follows (Fig. 1): The usual incision is made along the outer border of the erector spinæ muscles for about three and a half inches beginning just below the last rib. The fibres of the latissimus dorsi muscle are separated, the sheath of the quadratus lumborum muscle is opened in the direction of its fibres. The perirenal fatty capsule is exposed and incised, and by making gentle traction, particularly with each inspiration, assisted by rolling the patient downward on the inflated Edebohls bag, the kidney is delivered out of the wound and the fatty capsule dissected away. The surgeon then selects a position at the hilus of the kidney in the perirenal fascia which is free from bloodvessels, in the instance of the upper pole, about two centimeters from the pelvis and renal vessels, which he perforates with the blunt end of a long dressing forceps. Then an ordinary rubber drainage tube, one-fourth inch in diameter, with smooth surface, previously sterilized and of sufficient length to surround the kidney and protrude for some distance out of the wound when the kidney is replaced, is introduced through this opening made with the forceps (using the same forceps for this purpose) and clamped. Similarly, a second tube is introduced through the perirenal fascia, but this time at the extremity of the lower pole. To prevent the slipping of this tube over the end of the pole, care must be taken to pass it through such perirenal fascia as will not permit the slipping, or the tube is sutured with catgut to the perirenal fascia attachment of the kidney. The kidney is then gently replaced to what is about its normal position with the rubber tubes extending through the upper angle of the incision. The muscle and skin incision is then closed from below upward with continuous catgut suture leaving the tubes protruding through the extreme upper angle.

Without making the least traction on the rubber tubes, but being sure the kidney is in the position where it was placed, the tubes are gently tied over an oblong portion of gauze. Further, gauze is placed about and over the tubes and wound, then cotton to both sides of the spine, and the usual binder is applied.

The tube is placed over the lower pole in the position described and the ends of the tubes brought out at the upper angle of the incision so as to bring the kidney to and fix it in normal position, the upper two-thirds being beyond the twelfth rib.

The first dressing is made after three or four days, the tubes untied, and a new portion of gauze applied. The tubes, which easily slip out, are removed at the end of three weeks. The tubes remaining in this position for this length of time, it would be presumed, secure the formation of two connective-tissue tubes, then after the removal of the tubes, two connective-tissue cords, one surrounding the kidney above the hilus, from 2 cm. above the vessels obliquely downward, the other from the extremity of the lower pole in a slight oblique direction upward. The experimentation with the operation upon three dogs, however, demonstrates that this is not the actual result, as is shown in the illustration (Fig. 2). On the anterior surface of the kidney, the tubes having been removed three days previously, there are no adhesions, but the faintest trace of the line of tube can be detected. On the posterior surface, represented truly in the illustration, the adhesions extend between the capsule and quadratus lumborum muscle, the distance equal to the extreme upper and lower limits of the course of the tube tracts, possibly a little beyond this. The capsule is found to be as easily removed as in the case of the kidney of the opposite side, which was not operated upon, except that here and there will be found minute areas where it is slightly adherent. The underlying parenchyma, as shown by microscopic sections, is not injured, but normal. The capsule itself over the area of greatest adhesion, three days after the removal of the tubes, and three weeks and three days after operation, is increased one diameter in thickness. Elsewhere it is of normal thickness.

In the technique of this operation, as well as that of others, in making the incision care should be taken not to cut the iliohypogastric nerve. The kidney is to be delivered with the greatest care and gentleness by simply making traction on the fatty capsule, so as not to rupture or injure it. I would particularly emphasize that the principle of action of the rubber tubes is not, as some surgeons have seemed to understand, to make traction on the kidney and bring it firmly in contact with the quadratus lumborum muscle and incision, but they are to lie rather loosely about the kidney, steady it in position, and are to act simply as a foreign body, to produce mild irritation and the amount of adhesion described. Absolutely no traction is to be made upon them, which, if of any degree, would naturally cause a circular constriction and result in at least an acute albuminuria. This should never happen in the hands of any intelligent and experienced surgeon.

The amount of adhesion was the same in the instances of three dogs operated upon, and the strength of the attachment was sufficient to make it almost impossible by ordinary manual force to separate the muscle from the kidney capsule, which determines that it is likewise sufficient in man to permanently maintain the kidney in normal position. I have been able to demonstrate this fact within the last month while performing an abdominal operation on a woman upon whom five years ago I had performed nephropexy by this method. The kidney was found firmly fixed, with a slight range of mobility, perhaps a fourth of an inch in each direction.

The muscle and skin wounds heal by first intention, except for the line of tube tracts, which heals with the smallest cicatrix, within twenty-four hours after the removal of the tubes, as does any drainage tract under similar conditions.

The modification I present at this time is in the placing of the one rubber tube at the extremity of the lower pole so as to secure the kidney in a higher position, just below where it would be impinged upon by changes in the size of the liver, therefore, in normal position.

A modification of this operation was reported by Donaldson, of Los Angeles, Cal., as being performed by Johnson (*American Medicine*, February 28, 1903). The modification consists in making separate openings through muscle, fascia and skin for the end of each tube, in this way changing the direction of the tubes, the tubes not being in contact with the kidney capsule in that half of the circumference of the kidney toward the incision. I can see no advantage in this modification but believe it to be rather a disadvantage, for it is over this particular area on the posterior surface of the kidney that the strongest adhesion is formed. Also, there would be even more cicatricial change in five wounds than in one. He does not dissect away the fatty capsule, and provided a sufficient adhesion is attained, I am not sure that this would not be an additional protection to the kidney. We shall decide this question through experimentation within the next few weeks.

This operation has now been performed upon at least fifty cases, and a period of from seven and a half years to a few weeks have elapsed, and in no instance has a recurrence or symptom referable to the operation been reported. There has been no mortality, yet we must all admit that nephropexy is an operation requiring more experience and skill than the average abdominal operation. It requires experience to deliver the kidney out of the wound without

injury, the space of Garrotta is a field where infection would be very disastrous, there is danger of injuring the blood-vessels at the hilus and having severe hemorrhage, probably demanding nephrectomy, and the peritoneal or plural cavity may be opened, adding to the danger. The mortality in the hands of the experienced operator after the first few cases should not at most be more than 1 per cent.

I am indebted very greatly to Dr. P. G. Skillern, Jr., for his assistance in a thorough study of the literature which was necessary for the preparation of this paper.

A STUDY OF THE NATURE OF THE MICRO-ORGANISMS FOUND IN THE MOUTHS AND THROATS OF HEALTHY PERSONS.

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A study of the micro-organisms to be found in the mouths and throats of healthy persons was begun October, 1905, and since that time I have made more or less complete observations on twenty individuals who considered themselves to be in good health.

Streptococci and diplococci were found in every one of the twenty cases, so that basing the statement on these findings, it will be fair to say that streptococci and diplococci are contained in all healthy mouths.

Now it remains to be shown whether or not these streptococci are all the same variety, and furthermore the attempt has been made to show the same thing in regard to the diplococci and their relation to the organism which is the exciting cause of lobar pneumonia.

In carrying out the experiments in differentiating between the streptococcal and diplococcal forms the work has been along the lines, though not strictly adhering to the method, of Park and Williams' report to the Pneumonia Commission of New York.[1]

The characteristics which they give for differentiating between the different species are as follows:

I. (1) Typical pneumococci: Those cocci which under certain more or less constant cultural conditions occur principally in slightly elongated and pointed twos with their broader ends apposed:

(2) Under same or other cultural conditions form capsules;

(3) Produce coagulation when grown in inulin-serum medium;

(4) When grown on blood-agar plates produce a distinct green color in and about the colonies;

II. Atypical pneumococci: cocci which morphologically resemble more or less closely the pneumococcus, except in their growth in Hiss' inulin-serum medium.

Park and Williams further state that among the typical pneumococci all strains vary somewhat in their power to coagulate Hiss' inulin-serum medium, a few producing late coagulation, and that the non-coagulators which are more or less morphologically like the typical pneumococci are closely related to the typical late coagulators. All of the typical and atypical pneumococci with many strains of streptococci produce a green color in and about the colonies on blood-agar plates, while other streptococci produce only a zone of hæmolysis around the colonies, but no green color.

Schottmüller[2] obtained about the same results as did Park and Williams, and divided them into groups according to their growth on blood-agar. Streptococcus pyogenes produces hæmolysis, streptococcus viridens a green color and streptococcus mucosus mucous-like material as well as a green color.

Rosenow[3] obtained entirely different results, stating that no streptococcus he had tried produced a green color, though the pneumococcus did, and he recommended this as a differentiating test.

Park and Williams divide the typical pneumococci studied by them into several distinct morphological varieties:

1. Small cocci occurring under most cultural conditions in twos, and producing small capsules.

2. Large cocci occurring readily in short and medium length chains, and producing large capsules.

3. The so-called streptococcus mucosus.

The first two varieties are less distinctly bounded than the last which forms a definite morphological variety. This variety, which has been mentioned only a few times in literature, has been classed as a streptococcus under the name streptococcus mucosus, by Schottmüller, and streptococcus mucosus capsulatus by others. It is accompanied by the first variety of typical pneumococcus in cases of pneumonia patients and normal individuals; more frequently found in cases of pneumonia than in others.

These are classed as typical pneumococci for the following reasons:

1. On serum-free media after the first two or three generations it produces no mucus-like material and shows no capsule or chain formation, but appears as a typical pneumococcus.

2. It readily coagulates inulin.

3. It showed very distinct capsules in serum medium and in the blood of inoculated animals.

4. It has been found pure and in large numbers in two cases of lobar pneumonia.

5. The results obtained from absorption experiments (see Collins' report) indicate a close relationship between it and the typical pneumococcus of the second variety, while no relation is shown between it and the strains of typical streptococcus tested.

This has been given various names, such as streptococcus lanceolatus, var. mucosus, and diplococcus lanceolatus, var. mucosus; but Park and Williams have styled it simply "pneumococcus mucosus."

In the summary of Park and Williams' report they state that there are typical pneumococci present in the mouths of a large per cent. of all healthy persons, but that a higher per cent. of atypical forms were found in healthy persons than in those suffering from pneumonia.

Our own method of differentiating the species of diplococci and streptococci was somewhat of a modification of that of Park and Williams. All those organisms which appeared as elongated, pointed twos, with their broader ends apposed, which formed capsules on serum media, which coagulated inulin, not forming chains, or at least the elements of whose chains were limited to four, we called "typical pneumococci."

"Atypical pneumococci" were divided into two classes: Those which corresponded to the typical pneumococci as characterized above except that they did not coagulate inulin; and those which did not appear as elongated, pointed twos, with their broader ends apposed, otherwise being like the typical pneumococci.

Those were called "streptococcus mucosus" which formed capsules, coagulated inulin and arranged themselves in chains; or which did not form capsules though they coagulated inulin and formed chains; or those which formed capsules and long chains but did not coagulate inulin.

Streptococcus pyogenes did not form capsules, coagulate inulin, nor occur as elongated, pointed twos, with broader ends apposed, but appeared as coffee-bean-shaped diplococci, flat sides apposed, in long chains.

Blood-agar plates were not used in our experiments at all for differentiation of species.

Method. Material was obtained by means of a sterile swab from the mouths and fauces of healthy individuals. Immediately inoculations were made with one side of a swab upon two tubes of sterile Loeffler's blood-serum medium and upon eight or ten tubes of sterile agar slants in order to isolate the colonies by the serial tube method. With the other side of the swab several smears were made on as many sterile coverslips and examined directly, stained with Loeffler's alkaline methylene blue solution.

After twenty-four hours' incubation at 37.5° C., smears made from the blood-serum culture and from the first tube of agar were examined, staining with Loeffler's methylene blue. The mixed blood-serum culture was then plated out on agar so that any organisms which escaped isolation by the serial tube method might be isolated by the plate method. These plates were kept in the incubator for from twenty-four to forty-eight hours according to whether or not the colonies were sufficiently well developed within the shorter period.

This plan was followed in all subsequent efforts at isolation and examination, with the exception of a very few cases where plates were made immediately after inoculating one blood-serum and one agar tube and smearing on a sterile coverslip, by shaking the swab in sterile bouillon and then plating.

If a streptococcus or a diplococcus were found it was ascertained whether or not the organism possessed the power of coagulating inulin-serum medium and the presence of capsules or their absence, while growing in a serum medium was also determined. The inulin was allowed to remain at incubator temperature for four days after being inoculated, before determining the presence or absence of coagulation.

In the case of many of the first cultures the degree of acidity produced by the streptococcal and diplococcal forms was tested by growing them in a 2 per cent. glucose bouillon medium for ninety-six hours at a temperature of 37.5° C., and at the end of that time, titrating with $\frac{n}{10}$ solution of sodium hydroxide, using phenolphthalein as an indicator, as suggested by Duval and Lewis.[4] It was found, however, that the degree of acidity did not correspond with the coagulation of inulin, *i. e.*, the acid-formers of high degree by no means always coagulated inulin, nor was it found that a pneumococcus could be differentiated from a streptococcus on account of its greater acidity, for the streptococcus might show a greater acid production than an inulin coagulating pneumococcus. Therefore, after a few trials with glucose bouillon as a differentiating agent, its use was discontinued, because it showed nothing.

The methods used for capsule staining were the glacial acetic acid method of Welsh, Gram's method, and the method employed by Leo Buerger in his "Studies of the Pneumococcus and Allied Organisms with Reference to their Occurrence in the Human Mouth."[5]

Summary of Results Obtained in Each Case.

Date.	Source.	Organisms found on coverslip.	Organisms found on agar slant from swab.	Organisms found on blood serum from swab.	Isolated. org.
1905 Oct. 20.	J. B. R., no history of pharyngitis or tonsilitis	Singly grouped; thick rods, round ends; a few slender rods in pairs, tetrads; diplococci, long thin rods.	Streptococci in long chains; diplococci; rod forms in pairs.	Numerous streptococci in long chain diplococci (large); tetrads; a few rods in pairs and singly.	1, 2.
Oct. 24.	J. H. D.; med. insp.; no history of tonsilitis; frequently has simple angina.	Single, long thin rods; a few short, paired rods; tetrads and diplococci.	Streptococci; diplococci; paired rods, long, thin, single rods, a few tetrads.	Streptococci; large diplococci; short paired rods; tetrads.	1, 2, 3, 6, 7.
Oct. 28.	W. A. P.; janitor in laboratory. Slight pharyngitis due to cold and excesive smoking.	Many diplococci; a few streptococci; many staphylococci.	Long rods; diplococci; streptococci; staphylococci.	Same as on agar.	5, 8, 9, 10, 11, 2.
Oct. 25.	J. B. K.; between teeth	Many spiral forms; long and short rods; diplococci and tetrads.	No spiral forms; otherwise same.	No spiral forms; otherwise same as on coverslip.	5, 1, 14, 12,
Dec. 2.	S. D.; throat.	Numerous medium long, thick rods; a few diplococci.	Same as seen on coverslip.	Same as on agar.	1, 2, 3, 8.
Dec. 7.	D. R. S.; throat.	Short, round-ended rods; large and small diplococci.	Same as on coverslip.	Same as on agar.	1, 4, 5, 23.
1906. Feb. 8.	J. B. U.; med. student.	Bacilli in twos; diplococci; streptococci.	Same as on coverslip.	Same as on agar.	1, 2, 8, 13.
Feb. 19.	A. R. W. med. student.	Large and small diplococci; short rods in twos; single long rods, long, thread-like organisms; streptococci.	Streptococci; diplococci; tetrads.	Same as on agar.	1, 15, 3, 2.
Mar. 1.	C. S.; med. student.	Medium length; thick rods; short thick rods in twos; diplococci and streptococci.	Bacilli; streptococci; diplococci.	Same as on agar.	1, 2, 17, 15.
Mar. 10.	A. P.; school boy.	Long, slender bacilli; long, thick bacilli; medium length rods in twos; diplococci; strep.; staph.	Diplococci; streptococci; staphylococci.	Streptococci; staphylococci.	1, 2, 3, 5.
Mar. 21.	H. M. W.; med. student.	Diplococci and streptococci.	Same as on coverslip.	Same.	2, 3, 4.
Mar. 23.	V. D. McN.; med. student.	In twos; short, broad rods; encapsulated; diplococci; small diplococci; a few spirals; thin, medium length rods; singly and in twos.	Large, round-ended rods in twos; striated rods; streptococci; diplococci; a few lanceolate diplococci.	Same, plus a few very long rods.	1, 2, 3, 8.
Apr. 5.	A. M.; dental student.	Diplococci; streptococci; medium length rods.	Same as on coverslip.	Same.	1, 3, 5, 14, 15, 18, 19.
Apr. 11.	T. G. K.; med. student.	Thick rods; granular protoplasm; singly and in short chains; thin rods singly; diplococci; streptococci and spirals.	Medium rods; diplococci and streptococci.	Same as on agar.	1, 2, 20.
May 4.	W. F. S.; med. student.	Short, thick rods in twos; diplococci and streptococci; rods in short chains.	Encapsulated diplococci and streptococci; diplococci and streptococci not encapsulated	Large and small diplococci; streptococci.	1, 2, 15.
May 5.	H. L. B.; physician.	Long, thin spirals; long, medium thick rods; short, medium thick rods; diplococci and streptococci; short striated rods in squads of three or four.	Many streptococci; large and small diplococci; tetrads; a few short rods.	Leptothrix; many diplococci and streptococci.	1, 2, 4, 21.
May 9.	H. A. G.; med. student.	Diplococci; single medium length rods; long rods in twos; large round diplococci; square ended rods in short chains.	Streptococci; tetrads.	Streptococci; diplococci	1, 3, 13, 12, 15.
May 10.	R. E. C.; med. student.	Diplococci; short thick rods; medium length thin rods; long slender rods; striated rods.	Streptococci; diplococci; tetrads; short thick rods.	Streptococci; diplococci; short thick rods.	1, 5, 15.
May 17.	M. G.; med. student.	Diplococci; streptococci; medium sized rods.	Streptococci; tetrads; diplococci.	Diploc.; streptoc.; very short rods, with rounded ends.	1, 2, 3, 15, 22.
May 19.	W. M. S.; med. student.	Diplococci; streptococci; long rods; medium length rods; staphylococci.	Streptococci and diplococci; very slender medium length rods; tetrads.	Streptococci and diplococci; tetrads; short rods; streptothrix.	1, 2, 4, 14, 11, 15

In this work it was thought that a report on the diastatic enzymes produced by bacteria found in the healthy mouth might be of interest and perhaps instructive. Consequently a starch medium consisting of 15 grams of starch, 10 grams of peptone, 5 grams of sodium chloride dissolved in 1 liter of water was sterilized and employed for this purpose.

Distinguishing Characteristics of the Organisms.

Source of culture.		Occurring as elongated pointed rods with broader ends apposed.	Form capsules.	Coagulate inulin-serum medium.	Produce green color on blood-agar plates.	Occurring as coffee-bean-shaped diplococci.	Cocci in chains.	Name of organism.
Pneumococcus: typical.		+	+	+	+	—	—	
Pneumococcus: atypical (*a*).		+	+	—	+	—	—	
atypical (*b*).		—	+	+	+		—	
Streptococcus: mucosus.		—	+	+	+	+	+	
pyogenes.		—	—	—	—	+	—	
J. H. D.	1	—	—	+	..	..	—	Streptococcus mucosus.
J. H. D.	5	—	—	—	..	..	+	Streptococcus pyogenes.
J. H. D.	11	+	—	+	..	..	—	Atypical pneumococcus.
W. A. P.	10	—	+	+	..	+	+	Streptococcus mucosus.
T.	1	—	—	—	..	+	—	Streptococcus pyogenes.
S. D.	1	—	+	—	..	+	—	Atypical pneumococcus.
S. D.	3	—	—	+	..	+	+	Streptococcus mucosus.
S. D.	4	—	—	—	..	+	+	Streptococcus pyogenes.
D. R. S.	1	—	—	—	..	..	+	Streptococcus pyogenes.
D. R. S.	3	+	+	+	..	+	—	Typical pneumococcus.
J. B. N.	3	—	—	+	..	+	+	Streptococcus mucosus.
J. B. N.	4	—	—	—	..	—	+	Streptococcus pyogenes.
A. R. W.	1	—	+	—	..	+	—	Atypical pneumococcus.
A. R. W.	3	—	—	—	..	—	+	Streptococcus pyogenes.
A. R. W.	8	—	—	+	..	+	—	Atypical pneumococcus; 1 c.c. did not kill mouse; 2 c.c. killed mouse in three days.
A. R. W.	12	—	—	+	..	—	+	Streptococcus mucosus.
C. S.	1	—	—	+	..	+	+	Streptococcus mucosus.
C. S.	5	—	—	—	..	+	+	Streptococcus pyogenes.
A. P.	1	—	—	+	..	+	—	Atypical pneumococcus; 1 c.c. killed mouse in two days.
A. P.	2	—	—	—	..	+	+	Streptococcus pyogenes.
A. P.	7	+	—	+	..	+	+	Streptococcus mucosus.
H. M. N.	1	+	—	+	..	+	—	Atypical pneumococcus; killed mouse in two days.
H. M. N.	4	+	+	+	..	+	—	Typical pneumococcus.
H. M. N.	10	—	+	+	..	+	++	Streptococcus mucosus.
V. D. McN.	1	—	+	+	..	..	+	Streptococcus mucosus.
V. D. McN.	2	+	+	+	..	..	—	Atypical pneumococcus.
V. D. McN.	19	—	—	—	..	+	+	Streptococcus pyogenes.
A. M.	1	—	—	+	..	+	+	Streptococcus mucosus.
A. M.	7	+	+	—	..	+	—	Atypical pneumococcus.
A. M.	9	+	..	+	..	+	—	Typical pneumococcus.
T. G. K.	2	—	—	—	..	+	+	Streptococcus pyogenes.
T. G. K.	3	—	+	—	..	—	+	Streptococcus mucosus.
W. F. S.	1	—	+	—	..	+	++	Streptococcus mucosus.
W. F. S.	6	—	—	—	..	+	+	Streptococcus pyogenes.
H. L. B.	1	—	—	—	..	+	+	Streptococcus pyogenes.
H. L. B.	5	+	..	+	..	+	3 or 4 elem'ts	Typical pneumococcus.
H. L. B.	10	—	—	+	..	+	—	Streptococcus mucosus.
H. A. G.	1	+	+	—	..	—	—	Atypical pneumococcus.
R. E. C.	6	—	—	—	..	—	++	Streptococcus pyogenes.
R. E. C.	9	+	+	—	..	—	—	Atypical pneumococcus.
M. G.	1	+	—	—	..	..	+	Atypical pneumococcus.
M. G.	7	—	—	—	..	—	+	Streptococcus pyogenes.
M. G.	8	—	—	+	..	—	+	Streptococcus mucosus.
W. M. S.	2	+	+	..	..	..	—	Typical pneumococcus.
W. M. S.	6	—	+	..	..	..	++	Streptococcus mucosus.
W. M. S.	8	—	—	—	..	+	+	Streptococcus pyogenes.

Action of Organisms on Starch.

No.	Name.	Starch unchanged.	Amylodextrin.	Erythrodextrin.	Achroodextrin.	Maltodextrin.	Maltose.	Dextrose.
J. H. D.	1	Streptococcus mucosus.	−	−	−	−	−	+	−
J. H. D.	3	M. tetragenus.	+	−	−	−	−	−	−
J. H. D.	5	Streptococcus.	+	−	−	−	−	−	−
J. H. D.	6	Ps. trommelschlägel.	−	−	−	−	−	+	−
J. H. D.	11	Atypical pneumococcus.	+	+	−	−	−	+	−
W. A. P.	1	B. breslaviensis.	−	−	−	+	−	+	−
W. A. P.	3	Streptothrix asteroides.	−	−	−	−	−	+	−
W. A. P.	4	M. aureus.	−	−	−	−	−	+	−
W. A. P.	7	B. alcaligenes.	−	−	+	−	−	+	−
W. A. P.	10	Streptococcus mucosus.	−	−	+	−	−	+	−
W. A. P.	11	B. mesentericus.	−	−	+	−	−	+	−
T.	1	Streptococcus.	+	−	−	−	−	+	−
T.	2	M. aureus.	+	−	−	−	−	+	−
T.	5	B. ginglymus.	+	−	−	−	−	+	−
T.	7	Sarc. lutea.	+	+	−	−	−	+	−
T.	8	B. pseudodiphtheriæ.	−	+	−	−	−	−	−
S. D.	1	Atypical pneumococcus.	−	+	−	−	−	−	−
S. D.	2	M. tetragenus.	+	−	−	−	−	−	−
S. D.	3	Streptococcus mucosus.	+	+	−	−	−	−	−
S. D.	4	Streptococcus.	+	−	−	−	−	−	−
S. D.	13	B. mesentericus.	+	−	−	−	−	−	−
D. R. S.	1	Streptococcus.	−	−	−	−	−	−	−
D. R. S.	2	M. albus.	−	−	−	−	−	+	−
D. R. S.	3	Typical pneumococcus.	−	−	+	−	−	−	−
D. R. S.	6	M. aureus.	−	−	+	−	−	−	−
D. R. S.	8		−	−	−	−	−	−	−
J. B. N.	3	Streptococcus mucosus.	−	−	−	−	−	−	−
J. B. N.	4	Streptococcus.	−	−	−	−	−	+	−
J. B. N.	14	B. mesentericus.	−	−	−	−	−	−	−
J. B. N.	15	B. subtilis.	+	−	−	−	−	−	−
J. B. N.	16	Diploc. in chains.	−	−	−	−	−	−	−
A. R. W.	1	Atypical pneumococcus.	−	−	−	−	−	−	−
A. R. W.	3	Streptococcus.	−	−	−	−	−	−	−
A. R. W.	4	M. tetragenus.	−	+	−	−	−	−	−
A. R. W.	8	Atypical pneumococcus.	−	+	−	−	−	−	−
A. R. W.	12	Streptococcus mucosus.	−	−	−	−	−	+	−
A. R. W.	16	B. acidum.	−	−	−	−	−	−	−
C. S.	1	Streptococcus mucosus.	−	−	−	−	−	−	−
C. S.	5	Streptococcus.	−	−	−	−	−	−	−
C. S.	6	M. tetragenus.	−	+	−	−	−	−	−
C. S.	7	Bact. tiogense.	−	−	−	−	−	−	−
A. P.	1	Atypical pneumococcus.	+	−	−	−	−	−	−
A. P.	2	Streptococcus.	+	−	−	−	−	−	−
A. P.	4	M. aureus.	+	−	−	−	−	−	−
A. P.	6	M. albus.	−	−	−	−	−	−	−
A. P.	7	Streptococcus mucosus.	−	−	−	−	−	−	−
H. M. W.	1	Atypical pneumococcus.	−	−	−	−	−	−	−
H. M. W.	4	Typical pneumococcus.	−	−	−	−	−	−	−
H. M. W.	10	Streptococcus mucosus.	−	+	−	−	−	−	−
V. D. MeN.	1	Streptococcus mucosus.	−	−	−	−	−	−	−
V. D. MeN.	2	Atypical pneumococcus.	−	−	−	−	−	−	−
V. D. MeN.	11	B. mesentericus.	−	−	−	−	−	−	−
V. D. MeN.	19	Streptococcus.	−	−	−	−	−	−	−
A. M.	1	Streptococcus.	−	−	−	−	−	−	−
A. M.	6	B. typhosus *.	−	−	−	−	−	−	−
A. M.	7	Atypical pneumococcus.	+	−	−	−	−	−	−
A. M.	9	Typical pneumococcus.	−	−	−	−	−	−	−
A. M.	10	M. vincenzii.	−	−	−	−	−	−	−
A. M.	12	M. tetragenus.	−	−	−	−	−	−	−
A. M.	2	M. aureus.	−	−	−	−	−	−	−
A. M.	4	B. cereus.	−	−	−	−	−	−	−
A. M.	8	B. pseudodiphtheriæ.	−	−	−	−	−	−	−
T. G. K.	1	Bact. nasalis.	−	−	−	−	−	−	−
T. G. K.	2	Streptococcus.	−	−	−	−	−	−	−
T. G. K.	3	Streptococcus mucosus.	+	−	−	−	−	−	−
W. F. S.	1	Streptococcus mucosus.	−	−	−	−	−	−	−
W. F. S.	3	M. tetragenus.	+	−	−	−	−	−	−
W. F. S.	6	Streptococcus.	+	−	−	−	−	−	−
H. L. B.	1	Streptococcus.	+	−	−	−	−	−	−
H. L. B.	5	Typical pneumococcus.	−	−	−	−	−	−	−
H. L. B.	10	Streptococcus mucosus.	−	−	−	−	−	−	−
H. L. B.	11	B. megatherium.	−	−	−	−	−	−	−
H. A. G.	1	Atypical pneumococcus.	−	−	−	−	−	−	−
H. A. G.	3	Sarc. lutea.	−	−	−	−	−	−	−
H. A. G.	4	M. tetragenus.	−	−	−	−	−	−	−
H. A. G.	6	B. levans.	+	+	−	−	−	+	−
R. E. C.	1	M. tetragenus.	+	+	−	−	−	+	−
R. E. C.	6	Streptococcus.	+	+	−	−	−	+	−
R. E. C.	9	Atypical pneumococcus.	+	+	−	−	−	−	−
M. G.	1	Atypical pneumococcus.	+	−	−	−	−	+	−
M. G.	2	M. tetragenus.	+		−	−	−	+	−
M. G.	5	Bact. czaplewski.	+	+	−	−	−	+	−
M. G.	7	Streptococcus.	+	+	−	−	−	+	−
M. G.	8	Streptococcus mucosus.	+	+	−	−	−	+	−
W. M. S.	1	M. tetragenus.	+	+	−	−	−	−	−
W. M. S.	2	Typical pneumococcus.	+	+	−	−	−	−	−
W. M. S.	6	Streptococcus mucosus.	+	−	−	−	−	−	−
W. M. S.	8	Streptococcus.	+	+	−	−	−	−	−
W. M. S.	10	B. pseudodiphtheriæ.	+	+	−	−	−	−	−

KEY.

1 = Streptococcus pyogenes.	13 = B. subtilis.
2 = Streptococcus mucosus.	14 = B. pseudodiphtheriæ.
3 = Atypical pneumococcus.	15 = M. tetragenus.
4 = Typical pneumococcus.	16 = Bact. acidum.
5 = M. aureus.	17 = Bact. tiogense (Wright).
6 = Ps. trommelschlägel.	18 = B. cereus.
7 = Sarc. subflava (Ravenel).	19 = M. vincenzii.
8 = B. mesentericus.	20 Bact. nasalis.
9 = B. alcaligenes.	21 = B megatherium.
10 = B. breslaviensis.	22 Bact. czaplewskii.
11 = Streptothrix.	23 = M. albus.
12 = Sarcina lutea.	

The organism was inoculated into a tube containing about 10 c.c. of the medium and incubated at 37.5° C. for four days. Then it was tested for diastatic enzymes as suggested by A. MacFadyen and T. L. Brunton,[6] as follows:

1. Original starch } on addition of a drop of tr. iodi gives a
2. Amylodextrin } blue color.
3. Erythodextrin + iodine gives a red or violet color.
4. Achroodextrin } maltodextrin } cause no change when iodine is added.
5. Maltose reduces Fehling's solution but does not reduce Barfoed's reagent.
6. Dextrose reduces both Fehling's solution and Barfoed's reagent.

MacFadyen and Brunton tested Koch's and Finkler's spirilla, the scurf bacillus, and the Welford bacillus, as well as the "putrefactive micrococcus" in this way for diastatic enzymes, and concluded that the "same germ can produce both diastatic and peptonizing ferments."

In working along this line by this means no differentiation of species could be determined, but it was interesting to note that nearly all the bacteria in the same throat acted in the same manner toward the conversion or non-conversion of the starch solution, while those of the same species, from another throat, might act differently.

SUMMARY.

1. All of the throats examined contained streptococci and diplococci, showing them to be normal inhabitants of the normal mouth and throat.

2. Streptococcus mucosus was found in 70 per cent. of all cases.

3. Atypical pneumococcus occurred in 50 per cent. of the twenty cases.

4. Typical pneumococcus was present five times or in 25 per cent. of the number of cases examined.

5. Organisms of the same species may behave differently in their action on starch if the organisms are from different sources.

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BOOK REVIEWS.

Neurotic Disorders of Childhood: Including a Study of Auto and Intestinal Intoxications, Chronic Anæmia, Fever, Eclampsia, Epilepsy, Migraine, Chorea, Hysteria, Asthma, etc. By B. K. Rachford, Professor of Diseases of Children, Medical College of Ohio, University of Cincinnati; Pediatrist to the Cincinnati, Good Samaritan and Jewish Hospitals; Member of American Pediatric Society, etc. E. B. Treat & Co., New York.

At the present day of books on laboratory technique and diagnosis, it is a pleasure to get hold of a volume written with the purpose of Rachford's: to study the physiological peculiarities of the immature nervous system of infants and children, and to note the all-important bearing which these peculiarities have in producing and giving individuality to the neuroses of childhood. Infants and children are especially predisposed to serious and complicated nervous disorders, but this class of diseases is very little understood by the general practitioner, nor has it been a matter of special study by neurologists. The book consists of two parts. The chapters of Part I deal with the physiology of the nervous system, the physiological factors responsible for the high fevers and the variability of the temperature of children, the various toxæmiæ and anæmiæ. In Part II individual neuroses, as enuresis, chorea, epilepsy, eclampsia, hysteria, migraine, etc., are treated. Each disease is given careful consideration; its etiology, symptomatology, prognosis, and diagnosis being treated very fully, but it is especially in the description of the treatment of these conditions where the book excels. Never have we seen in a book of its size such complete essays on the treatment of each one of the diseases under discussion. We should like, in particular, to call attention to the chapter on enuresis; the observing power and vast experience of the author are mirrored in the description of this troublesome neurosis. In another chapter he relates case histories, showing the intimate relationship of recurrent vomiting, recurrent coryza, toxic epilepsy and migraine; all of them in his opinion are autointoxications, and probably due to the same autotoxins. Suggestion is the most potent factor, both in the production and cure of hysteria. A perusal of the book will aid the general practitioner to better comprehend these diseases, and will enable him to apply successful lines of treatment. E. L.

Ophthalmic Neuromyology. A Study of the Normal and Abnormal Actions of the Ocular Muscles from the Brain Side of the Question. By G. C. Savage, M.D., Professor of Ophthalmology in the Medical Department of Vanderbilt University. Thirty-nine full-page plates and twelve illustrative figures. Published by the author.

The author says of his book, that it makes the muscle study of the eyes easy, and, this being so, it would seem to us as if it would be a useful book for every physician doing refraction work. The author certainly has gone into the subject sufficiently in detail to satisfy the most knowledge-loving man among ophthalmologists. E. L.

Lectures on Tropical Diseases. Being The Lane Lectures for 1905, delivered at the Cooper Medical College, San Francisco, U. S. A., by Sir Patrick Manson.

The lectures discuss the general principles of the distribution of tropical diseases, and contain the important advances in tropical pathology, with methods for the recognition and treatment of diseases peculiar to warm climates. The disease germs peculiar to warm climates are classified into groups, based upon the effect of climate upon their life history and the natural history of the disease. The diagnosis and treatment of tropical fevers and fluxes are considered from a practical clinical standpoint. The problems in tropical medicine relating to the island possessions of the United States are briefly presented. The subject is interesting, and the personal knowledge of the lecturer compels attention. The book is well made and carefully illustrated. V. N.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

James Tyson, M.D., Professor of Medicine.

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PERINEPHRITIS AS A CAUSE OF SYMPTOMS SIMULATING THOSE OF STONE IN THE KIDNEY.[1]

By James Tyson, M.D.,
Professor of Medicine, University of Pennsylvania.

By perinephritis I mean an inflammation of the capsule and other tissues surrounding the kidney, of such nature as to produce contraction or cicatricial markings in the capsule, whence also the cortex of the kidney may be more or less invaded. The term *paranephritis* may be applied to more distant peripheral inflammation, including suppurative processes due to stone and other causes. Few physicians of large experience have failed to meet cases with symptoms of nephrolithiasis including continuous or paroxysmal pain in the region of one kidney radiating into the abdomen, groin and inside of the thigh and sometimes associated with pyuria, for which operation has been recommended and performed without finding stone; this, too, after the most searching examination, including section of the kidney.

What was at the time even more surprising, such operation has not infrequently been followed by relief of symptoms, even though the stone has not been found. Such at least had been my experience several times before a case occurred to me which suggested an explanation. This was the first case to be reported, that of a lady who consulted me for albuminuria in 1893 before marriage. She was then twenty years old. She had three children without serious complications. For some time prior to October, 1903, while under the care of Dr. Radcliffe Cheston, she suffered with painful attacks in the left kidney accompanied by moderate pyuria, which was intermittent. The attacks became so severe and numerous as to suggest operation for her relief. She had also had recurring attacks of appendicitis. I was asked to see her in consultation with Dr. Cheston and Dr. John G. Clark. I examined her at the University Hospital, October 13, 1903, and found marked tenderness in the region of the left kidney brought out by pressure on the eleventh and twelfth ribs —distinct tenderness—extending down in the course of the ureter. She reported that she had much pain in this vicinity especially when active. There was also pain in the region of the appendix of a "dragging" character, worse when she was on her feet. Examination of urine failed to find albumin, but there were a few hyaline casts, and while there cannot be said to have been pyuria there was more than the normal number of leukocytes.

Dr. Clark operated. The left kidney was found closely anchored underneath the diaphragm by dense adhesions which made it difficult to release and deliver it upon the surface. On splitting and laying back the fibrous capsule the surface of the kidney appeared normal except at the upper pole, where it was densely adherent to its capsule. In like manner the cut surface of the longitudinal section appeared normal to the naked eye. The kidney itself proved to be smaller than normal and there may have been some interstitial nephritis responsible for the albumin and casts found many years ago, previous to her marriage. No evidence of a stone or tuberculosis was found. The upper pole of the kidney was lobulated and presented a number of cicatricial-like markings, though it could not be asserted positively that these cicatrices were not marks of congenital lobulation. But in view of the adhesions in this part and their absence elsewhere it seems reasonable to regard the markings as pathological rather than embryological. A strip of gauze was lightly packed in upon the dorsum of the kidney in order to promote adhesion between its surface and the dorsal wall. At the same time as the renal operation an appendectomy was done for the patient. She made a good recovery and has had no return of the painful symptoms. I append the histories of four additional cases.

The second case I saw presented itself a few months after the first patient. The symptoms were sufficiently similar to justify a like diagnosis. Dr. E. E. Montgomery operated and found firm adhesion between the colon and the perirenal fat of the left kidney, requiring considerable force to separate the fat from the capsule. Dr. Montgomery decapsulated both kidneys down to the pelvis and utilized the capsule in anchoring the kidney to the muscular structure. The patient also did well and has been relieved of her symptoms. Her own statement is that she has not been so well for years and no longer considers herself an invalid.

The other case from Dr. Clark's clinic, as will be seen by the history, was one of typical nephritic colic in which operation found no stone after sagittal section of the kidney and examination of the ureter with the sound. The kidney was, however, found enlarged and very adherent to its fatty capsule. Relief up to the present time has been complete.

Case I.—In February, 1893, I was asked to see with Dr. E. W. Griscom a young lady of twenty, engaged to be married,

[1] Read before the Association of American Physicians, May, 1906.

in whom was found a copious albuminuria. Miss P. had enjoyed excellent health up to three years before I saw her, when she became nervous and hysterical. She spent a year in Europe, from August, 1890, to May, 1891, without any improvement. She consulted Dr. Griscom on her return who found the albumin but no casts. At my visit the girl appeared quite bright, with a good color and described herself as feeling well. My own examination found a trace of albumin in the morning urine and one-tenth plus in the evening urine, but no casts. Later, cylindroids were found and octohedra of oxalate of lime. She was not discouraged from marrying and did marry, and had three children without any untoward symptoms, though I was anxious lest the pregnancy aggravate the renal condition.

On October 13, 1903, ten years after I first visited her, I was asked to see her again in consultation with Drs. Cheston and Clark. In addition to the symptoms of appendicitis she had pain in the region of the left kidney with occasional discharges of pus and a corresponding quantity of albumin, alternating with periods of absence of pus. At my examination I found tenderness over the region of the kidney especially when the eleventh and twelfth ribs were pressed upon. This tenderness extended down the course of the ureter. She complained also of acute pain in this same region especially when active and on her feet. She was very uncomfortable also in the neighborhood of the appendix.

I examined her urine at that time and found no albumin but a few hyaline casts and a few more leukocytes than normal. There were also cuboid and cylindrical epithelial cells. Catheterization of the ureter from this kidney obtained some urine containing albumin, but this time no casts. Dr. Clark operated as above stated on the first of November with the findings reported.

Case II.—Mrs. D. L. B., aged forty-one years, mother of three children, youngest eleven years and the oldest twenty-one years of age. Enjoyed unusual good health up to two years ago when she began to feel great lassitude followed by pain in the back on the left side, between the edge of the ribs and the crest of the ilium, extending down into the left groin. The pain was persistent with paroxysms of greater severity lower down in the abdomen. She consulted Dr. Musser at that time and after a long period of rest was relieved of the pain. In the meantime an *x*-ray examination had been made twice with negative results. Dr. John G. Clark also saw her, catheterized the ureters twice and found some obstruction in the left.

The pain returned in the summer of 1903, and continued up to November 2, when she consulted me. She had lost in six weeks twenty pounds. At this time she appeared not an ill-looking woman and was well-nourished, but complained of more or less constant pain on the left side as located above. She was, however, better when in bed, the pain increasing as the day advanced, when she also became weary and exhausted. She was again relieved on lying down. The pain at this time was a dragging pain. She complained of a good deal of distress in her head, including a sense of weight which made it uncomfortable to wear her hat. There was a tenderness to pressure in the region of the left kidney.

Dr. Montgomery saw her in consultation and operated November 13, 1903. There was found quite a firm adhesion of the colon and perirenal fat to the left kidney, requiring considerable force to separate the fat from the capsule. Both kidneys had the capsule completely separated down to the pelvis of the kidney, and the capsule was utilized in anchoring the kidney to the muscular structure. Result, total relief to symptoms.

Case III.—For this case I am indebted to Dr. John G. Clark. Mrs. L. B., aged twenty-six years, had a negative family history and herself had the usual diseases of childhood, since which her health had been perfect. She had had one child living and well, the birth being without complications. About three years prior to October 30, 1905, began to have backache and dragging down sensations, headache, and dull, aching pain in both groins. Early in July, 1905, about 3 A M., patient was seized with violent pain in the region of the left kidney, was nauseated and vomited several times. She was relieved by hypodermics of morphine. She remained in bed about a month, the dull, aching pain continued in left kidney region all the time with attacks of sharp pain causing her to vomit. Of this she was only relieved by morphine. After several of these attacks of pain she had retention of urine and had to be catheterized; subsequently had incontinence. After some of these attacks patient says her urine was bloody and sometimes cloudy. The pain usually radiated downward and sometimes ran into the left thigh and was often so severe that it caused her to double up. After about a month's stay in bed patient arose, still having the dull pain in her side. About a month later she had another attack of sharp pain which confined her to bed for a few days. This attack was not so severe as the former. One month ago the patient had another similar attack but less severe.

The urine examination found the secretion amber-hued, clear, acid in reaction, with a specific gravity of 1024 and depositing a slight, flocculent sediment. There was no albumin, no sugar, while the microscope found no casts but a few red blood cells and a few leukocytes and triple phosphate crystals. On the third of November the ureters were catheterized. Catheterization was followed by extreme abdominal pain, relieved by hypodermic injections of codeine, morphine, and atropine, and a hot pack. Pain seemed to be general, at times worse on the left side, and while constant was also subject to exacerbations.

Examination of her urine removed by catheter from the right kidney found a few red blood cells; that removed from

the left kidney contained large numbers of red blood cells and visible blood but no tube casts. A Röntgen ray picture was taken the next day and was negative so far as evidences of stone were concerned. It was thought the kidney was enlarged, however, by reason of the enlarged shadow.

Dr. Clark operated November 6th. The left kidney was found enlarged and very adherent to its fatty capsule; also to the diaphragm and was delivered with considerable difficulty. The upper pole, indeed, was not delivered. Palpation of the kidney failed to reveal stone. Sagittal section of the kidney was then made down to the pelvis and the pelvis and calices examined with the finger while the sound was passed down into the ureter without finding calculus. From such examination as could be made under the circumstances the kidney seemed to be the seat of parenchymatous nephritis. It was returned and the wound suitably dressed.

For twenty-four hours after the operation the patient's urine was distinctly bloody and less so for a longer time. On the 25th the patient reported her pain all gone, although the urine still contained enough blood to be noted macroscopically. On examination it was found to have a specific gravity of 1021, to be acid in reaction, cloudy, reddish, and deposited a red, flocculent precipitate. There was an evident trace of albumin but no sugar. There were many red blood cells.

On December 4th the wound had healed completely, the kidney was in good position, there was no pain and the patient was discharged. Since patient returned home she reported by letter that she is still free from her old renal pain.

Case IV.—F. W. C., aged twenty-three years, of nervous temperament, a clerk by occupation, had good health until his seventeenth year, when he fell from the top of a school-house, striking "on all-fours." The accident was followed by bloody urine. Again, when twenty-two years, was thrown from a horse, the pommel of the saddle striking the epigastrium, producing bruising in that locality. For some time prior to August, 1905, there was so much pain in the vicinity of the gall-bladder that biliary calculus was suspected and operation done, when the appendix was found adherent to the gall-bladder but no gallstones were found. The appendix was removed and he never had return of pain in the hepatic region. Two weeks after the operation, which was done August 25, 1905, pain appeared in the region of the right kidney. The pain was so severe as to require morphine in pretty full doses hypodermically. On November 12, 1905, the kidney was cut down upon with the expectation of finding stone, but no stone was found. Dr. Floyd W. McRae, who did the operation, informs me that the kidney was surrounded by very dense adhesions, was drawn toward the median line and firmly against the under surface of the right lobe of the liver. It was impossible to deliver the kidney without splitting the capsule and decapsulating. He opened the pelvis of the kidney but found no stone. There was also a spot of pain low down in the ureter as though a stone were impacted there, but the ureter was explored with negative results.

Succeeding the operation the pain was relieved for four weeks when it recurred suddenly and severely in the region of the left kidney, just like that of nephritic colic and closely resembling the pain before the operation. This pain lasted an hour or until relieved by hypodermic injections. In twelve hours he had another similar attack and since then they come on at odd times while a dull throbbing continues between the paroxysms and he needs from three-quarters to one and three-quarter grains of morphine hypodermically in the twenty-four hours to keep the pain subdued. There was therefore some question as to whether there might be a morphine habit. To determine this I had him seen in consultation by Dr. Mills and Dr. Frazier. In view of the findings at the operation it was concluded that while the relief afforded by opening may have had some demoralizing effect, the paroxysms were nevertheless actual.

The fourth case was the only male out of four, and the only one of the four in which the right kidney was involved. It was traumatic and the lesions found at operation, viz., tough adhesion of the right kidney to the under surface of the liver, were in accord with their etiology and explained satisfactorily, in the light of other cases, the symptoms. The return of the latter after a period of relief succeeding operation was reasonably ascribed to a renewal of the adhesions. Dr. McRae writes me that it was his intention to remove the organ should the symptoms persist.

In view of these cases it is not unlikely that other gross pathological lesions of the kidney or ureter, such as tuberculosis, tumor, pyelitis, and hydronephrosis, may at times be responsible for like symptoms. The same may be true even of parenchymatous, interstitial, and glomerulonephritis of one side. The latter conditions must, however, be considered as very rare causes of the symptoms described.

Most interesting in this connection is the fact that the conditions referred to were recognized by the eminent French renal pathologist Rayer, in whose classic work published in 1839 a description of perinephritis covering several pages may be found. He says, "As a result of contusions or heat or cold and sometimes without any known cause, either during grave febrile affections or even good health, the cellular fatty cushion surrounding the kidney, inflames, becomes infiltrated with a seropurulent fluid or becomes the seat of abscess formation without the kidney itself participating in the process or suffering any appreciable derangement of its functions." Also, "In other cases blood may be extravasated between the kidney and the enveloping membrane, while at various points on the membrane purulent deposits or deposits of plastic lymph with ecchymoses may be seen, causing the

kidney to become adherent to the contiguous structures. Pus may even be found in the external cellular tissue, especially in that part corresponding to the posterior aspect of the kidney." Again Rayer says, "I feel constrained to remark here that this membrane sometimes adheres so forcibly to the cortex at its inferior surface, and to the adjacent structures by its external surface, that it is impossible to remove it without operative procedure. It should also be stated that the thickening, the cartilaginous and osseous changes of this membrane are not the result of age, but the result of preceding inflammations that have caused the deposit of plastic lymph or of salts either upon or within the membrane."

It is true Rayer lays greater stress on termination in suppuration which is not thought to have entered into the more insidious processes found in most of my cases. On the other hand, Case IV quite corresponds to the more serious conditions described by Rayer, while there may be recognized in his descriptions conditions corresponding to those in the milder case described by myself.

I must not fail to allude to a modern observer who has called attention to like conditions—Dr. Joseph Ransohoff, of Cleveland, who published[1] a case of "Unilateral Disease of the Kidney Simulating Stone," almost identical with some of those published in this paper, and on which he operated successfully, with relief to symptoms, by splitting the capsule and sectioning the kidney. He discusses the subject intelligently and recommends that when such cases simulating stone come to operation a small section of the kidney be removed for microscopic examination. This was done in his case, which proved to be one not of stone but of atypical glomerulonephritis with adherence of the capsule proper to the fat capsule. Among the symptoms were "microscopic hæmaturia," in addition to pain and tenderness, desire to urinate, etc. He also recommends a method of examination which I have found very satisfactory, viz., pressure by the thumb on the eleventh and twelfth ribs. This is conveniently practised with the patient leaning forward with the hands on the arms of the chair.

The rationale of relief afforded by splitting the capsule and section of the kidney is not far to seek, required relief of tension and pressure being thus secured.

CRYPTOGENETIC STREPTOCOCCUS INFECTION WITH PERSISTENT CUTANEOUS ERUPTION, ENLARGEMENT OF THE LYMPHATIC GLANDS AND FEVER SUGGESTING SYPHILIS.

By Alfred Stengel, M.D., J. William White, M.D.,

and

Joseph S. Evans, M.D.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

The report of the case which is the basis of this paper was prompted by the unusual clinical features and the results of bacteriologic study. The patient, a physician, had consulted a number of physicians, dermatologists, and syphilographers before consulting one of us (S). Various opinions had been expressed for and against syphilis. Our own belief in the non-syphilitic character of the disease seems to be confirmed by our bacteriologic studies, which appear sufficiently conclusive to justify publication. We are indebted to Professor James C. Wilson for the photographs of the case, which were taken when the patient consulted him, and to Professor Henry W. Stelwagon for photographs and a statement of the clincal features observed by him.

L. D. J., aged twenty-six years, does not remember having diseases of childhood and was in good health until fourteen years of age. At that time he had some form of gastrointestinal disorder with marked nervous symptoms and disturbances of vision. The nervous symptoms were attributed to a muscular disorder of the eyes and astigmatism. About the same time he developed a fissure in ano. After correction of the eyes and cure of the fissure his general health improved and he was practically well. At eighteen he began to prepare for his medical studies and finally graduated at twenty-five. He was a resident physician in one of the hospitals and while there was perfectly well until June 1, 1905.

The following account of his condition from the onset of that trouble until he first consulted me (S) was prepared by a medical friend who was constantly associated with him during the time.

History of Present Illness. In the latter part of May, 1905, the patient began to complain of digestive disturbances, sore throat, and lassitude. He being slightly jaundiced, vomited occasionally, and had no desire for food. He also complained of an intense itching of the skin. At this time an eruption which looked exactly like seborrhœic eczema made its appearance upon the ankles, thighs, buttocks, back, and elbows. This eruption appeared in fairly well-defined patches.

[1] Journal of the American Medical Association, May 30, 1903.

Examination of the throat, made upon several occasions, showed the posterior pharyngeal wall to be dry and congested, with an enlarged follicle here and there over its surface. The tonsils were also somewhat inflamed and slightly enlarged.

The patient was placed on a reduced diet, given sodium phosphate internally, and ordered a warm alkaline bath at bedtime. Slight improvement followed the treatment. In the middle of June he went to the country for two weeks. Upon his return he stated that he felt no better.

From July to the middle of September his condition varied from week to week, although during this period he never felt in his normal condition. The eczematous rash faded markedly and in some places disappeared entirely. Slight jaundice developed. The patient states that at this time he had several sharp chills followed by free sweating. In the meantime an erythematous rash broke out on the arms, thorax and abdomen, and later invaded the lower extremities. After the patient returned to Philadelphia early in November his condition became constantly worse. The pain in the region of the sternum extended over the entire anterior thoracic region, the dyspnœa became severe, the axillary glands continued to enlarge and become more and more painful. The other lymphatic glands, notably the inguinal group, likewise became affected. The patient had an evening temperature of 100° to 102° F., with profuse sweating at night, and was distressed by the constantly increasing dyspnœa and the

Fig. 1.—The eruption in its earlier stages. (From a photograph taken for Dr. J. C. Wilson.)

Fig. 2.—The eruption in the later stages. (From a photograph taken by Dr. H. W. Stelwagon.)

was noticeable at times, nausea was experienced, and on several occasions vomiting occurring immediately after eating. The patient was nervous, irritable, and suffering from insomnia. In the latter part of September he complained of feeling much worse, "sick all over," as he himself expressed it, and about the first of October left again for the country, where he remained until November. During the month of October he became steadily worse, losing weight and strength, and suffering more and more from insomnia. The axillary lymphatic glands began to enlarge and were painful and sensitive to touch, there was more or less pain under the sternum, and dyspnœa, which became worse upon exertion, severe substernal pain. In short, he presented the appearance of one seriously ill. A blood count showed a leukocytosis of over 21,000. The rash which had become more and more marked assumed a multiform character, papules alternating with macules, etc.

The patient consulted several physicians, surgeons, and dermatologists in Philadelphia and New York, and finally entered a hospital, where he received the so-called mercurial therapeutic test in the form of hypodermic injections, there being a question as to whether his illness might not be the result of syphilitic infection. This treatment seemed to produce a slight fading of the rash, although the change was

not at all decided, and he himself doubted the occurrence of any noticeable alteration. Only a few injections were administered.

November 26, 1905. The patient first consulted me (S) on this date, when he gave substantially the history as above and in addition told me that he had had numerous attacks of tonsillitis. He also reported that in October, 1905, he began to have intense headaches after eating. After this he developed rheumatoid pains in his left shoulder, and on one occasion, after having drunk cold water at a mineral spring, he had a heavy shaking chill and continued chilly for about three days. It was after this that he first developed substernal pain and enlargement of the gland in his left axilla. There was also a constant aching sensation in his jaws followed by a swelling of the glands at the angle of the maxilla on the right side. The rash which he presented on first consulting me appeared about this time, first covering the abdomen and chest. There was none then on legs. He reported hyperæsthesia at various points but had no itching. There was a distinct tendency, however, to urticaria.

After the original chill there was some fever and this continued more or less steadily for three weeks; then subsided, the rash at the same time becoming marked. Subsequently each recurrence of the fever was attended with a distinct increase in the rash.

The glandular enlargement when I first saw him involved the post-auricular groups on both sides, the anterior cervical and both axillary groups, especially the axillary glands on the left side; both inguinal groups slightly and the supraclavicular on the left side.

The rash found at his first visit was a blotchy erythema and folliculitis, most marked over the abdomen and chest, some on the forehead, none on the arms or legs. He reported that there had been papules and miliarial vesicles but these were not present when I saw him. Physical examination at this time and subsequently disclosed no evidence of any visceral lesion. The thoracic and abdominal organs all appeared normal. Repeated palpation of the spleen failed to show any enlargement. The only pathological conditions discoverable were the pharyngitis and tonsillitis, the cutaneous eruption and the enlargement of the superficial lymphatic glands.

January 7, 1906. He presented himself on this day with a fresh outbreak of eruption, much of which was papular and minutely vesicular.

17*th*. The rash has subsided distinctly, apparently under the influence of salicylates.

27*th*. The rash is of dusky color but still quite evident. Glands remain about the same. He has been taking guaiacol carbonate and salicylates since January 7th.

The following clinical examinations were made under our direction:

Urine: Specific gravity, 1020; reaction, acid; no albumin; no sugar; microscopic examination, negative. Subsequent examinations gave similarly negative results.

Blood: The patient reported that there had been leukocytosis (21,000 and 17,000 per c.mm.) before he consulted us.

November 27, 1905. Leukocytes, 8880; polymorphonuclear, 73 per cent.; large mononuclear, 5 per cent.; transitional 2 per cent.; lymphocytes, 14.5 per cent.; eosinophiles, 4 per cent.; basophiles, 1.5 per cent.

January 17, 1906. Red corpuscles, 5,090,000; leukocytes, 8320; hæmoglobin, 65 per cent.; polymorphonuclear, 67.4 per cent.; large mononuclear, 4.4 per cent.; transitional, 5.6 per cent.; lymphocytes, 18.6 per cent.; eosinophiles, 1.8 per cent.; basophiles, 2.2 per cent.

March 26*th*. Red corpuscles, 5,730,000; leukocytes, 10,320; hæmoglobin, 95 per cent.; polymorphonuclear, 69 per cent.; transitional, 2.4 per cent.; lymphocytes, 19.8 per cent.; eosinophiles, 2.4 per cent.; basophiles, 0.8 per cent.

April 19*th*. Red corpuscles, 5,720,000; leukocytes, 6080; hæmoglobin, 90 per cent.

The patient reported that several examinations had previously been made to determine the presence or absence of the Spirochæta pallida. One observer had failed to find this organism either in the serum taken from the skin over the eruption or in one of the lymphatic glands which was excised for the purpose of examination. Another observer had reported the finding of a single spirochæta in the examination of a number of slides prepared from the serum obtained from the skin over the eruption. The slide in which this supposed spirochæta was found had been lost and the finding could not, therefore, be subsequently verified. Without such verification we think it permissible to question the finding in view of the previous negative report on the serum and juice of an excised gland and our own subsequent failure to find the organism in the serum drawn from the skin or in the juice drawn from a thoroughly kneaded lymphatic gland.

Stomach Contents, November 28, 1905. Total acidity, 25; free HCl, 18; no lactic acid.

Dr. Evans' bacteriological studies were as follows:

On January 23d a cultural examination of the patient's blood was made. Five cubic centimeters of blood were taken from a vein at the flexure of the elbow-joint, a point free from the cutaneous lesions being selected. Twenty tubes of melted agar cooled to 45° C. were inoculated and plates poured. At the end of twenty-four hours there was such marked evidence of contamination that the culture was discarded.

A second examination was made January 29th; ten cubic centimeters of blood were taken with the same precaution to avoid skin lesions. Five cubic centimeters of this were divided equally among five flasks of bouillon, each containing 200 cubic centimeters; the remaining blood was divided

among tubes of litmus milk for anaërobic cultures by the pyrogallic acid and sodium hydroxide method. The cultures were incubated in 37.5° C., and at the end of twenty-four hours there was a slight acidity in the milk. Sub-cultures were made from the flasks on slant agar, and twenty-four hours later a growth was found to have occurred in four of the flasks, the remaining one being sterile.

The organism in all four tubes was identical and proved to be a Gram-positive coccus, oval in shape occurring mostly in diplococcic forms but also found in chains of four and six. Division occurred in only one plane. A further description will be given later.

At the time the blood culture was made, smears were taken from the serum of the cutaneous lesions with the end in view of examining for the Spirochæta pallida, since previously there had been both a positive and negative report as to the presence of this organism. Our findings were negative.

The next day an enlarged axillary gland was massaged and a small quantity of the glandular juice withdrawn by a syringe. Artificial sodium hydroxide blisters were also made. Specimens of the glandular fluid and the serum of the blisters failed to reveal the presence of the Spirochæta pallida.

On March 27th a second blood culture was taken. At this time the patient was practically free from the cutaneous lesions. The only glandular enlargement was in the anterior cervical chains. The flask method was employed and subcultures showed growth in all five. Morphologically the organism was identical with the one isolated by previous culture.

On March 29th a culture was made from the depths of a large crypt in the tonsil. A mixed growth occurred, but one of the organisms was identical with that isolated from the blood. A systematic study of the cultural characteristics of the three organisms revealed only one difference. Culture No. 1 (isolated January 29th) produced slight acidity of litmus milk lasting for twenty-four hours, followed by an alkaline change, whereas culture No. 2 (isolated March 27th) and culture No. 3 (throat) produced permanent acidity. This difference, however, was thought to be due to the different ages of the three strains.

April 24th culture No. 1 (then three months old) and culture No. 2 (one month old) were again studied on the various media and exhibited identical characteristics. Culture No. 3 unfortunately became contaminated and was lost.

The following are the characteristics of this organism:

Morphology. Cocci, oval in form, occurring as diplococci and in chains of four and six. Division takes place in one plane and the elongation which precedes it sometimes is indistinguishable from a rod. There is a capsule especially when grown on blood serum. Involution forms are numerous.

Motility. None.

Temperature Requirements. Grows well at 37.5° on ordinary culture media; better on glycerin agar, blood serum and glycose agar; no growth at 20° or 28°.

Oxygen Requirements. Facultative anaërobe.

Gelatin. No growth either in plate or stab culture.

Glycerin Agar Plate. Superficial colonies are flat with an abrupt border and a deep dark central nucleus. They are homogeneous, translucent, grayish in color, and dew-like in appearance. Under the low power they appear irregularly round with rough edges, coarsely granular and light yellow in color. A short distance within the edge there is a greater degree of growth, from which ring it decreases both toward the centre and the true periphery (cross-section). The deep colonies are pin-head in size, irregularly round or whetstone shape with margins at first sharply defined but later showing irregular prolongations.

Stroke. Small, pale grayish, dew-like colonies. Marked growth in the water of condensation as a thick, white flaky sediment. In this sediment the cocci occur in longer chains and the capsule is more readily demonstrated.

Stab. Growth occurs along the entire length of the puncture as minute grayish, translucent colonies.

Potato. No visible growth occurs.

Blood Serum. Small grayish irregular colonies with slight tendency to confluence. A flaky cloudiness in the water of condensation.

Gas Production. None produced on glucose, saccharose or lactose media. Growth abundant along the entire length of the stab.

Litmus Milk. Slight acidity for twenty-four hours, then progressively increasing alkalinity. No coagulation.

Bouillon. The organism grows as a whitish, flocculent sediment, the medium remaining clear. Later the sediment becomes confluent and when the medium is shaken rises up from the bottom as a thread.

Staining. Stains by ordinary aniline dyes and by Gram's method. Optimum growth occurs on glycerin agar, glucose agar, and blood serum.

Pathogenesis. Was non-pathogenic to rabbits and guinea-pigs when inoculated in large doses intravenous, intraperitoneal and intrapleural. Slight temporary inflammation took place at the site of subcutaneous injection. White mice inoculated subcutaneously sickened and lost weight, an abscess forming at the side of inoculation. When given plenty of sunlight and fresh air the animals recovered in two to three weeks. 2 c.c. of a suspension of the culture having a cloudiness equal to a twenty-four-hour typhoid bouillon culture injection into the inner surface of the right thigh of a ring-tail monkey produced in twenty-four hours an inflammatory reaction at the site of injection which continued for five days without producing suppuration. Three days after inoculation the right inguinal glands became slightly enlarged. Six days later they became

markedly enlarged and there was noticed some enlargement of the left inguinal and right axillary glands. Four days later the left axillary glands could be palpated. The monkey did not apparently sicken. This glandular enlargement began to lessen at the end of four weeks and entirely disappeared at the end of twelve weeks.

We believe this organism to be one of the streptococcus group, because it divides in one plan and occurs in encapsulated chains. Notwithstanding the present tendency on the part of many observers to look upon the various streptococci found in different pathological conditions as being in reality the same organism modified in some of its characteristics we consider that this organism is distinct from the pyogenes variety or from the Streptococcus pneumoniæ. It resembles the latter because of the predominance of the diplococcic forms, but the character of the growth on agar and the size, shape, and consistence of the colonies are entirely different. The appearance of the colonies under the low power of the microscope, *e. g.*, the sharply defined edge and the concave centre, the production of an alkaline reaction and the absence of coagulation in milk, even in the first sub-culture, distinguishes it rather sharply from the pyogenes variety. The characters of the organism isolated by Schütz, Saud, Jensen and others from horses suffering with contagious coryza and glandular enlargement agree most closely with those found in the examination of our organism. We make this comparison, however, not to identify the organism isolated from our case with that of Schütz, but merely to state our belief that we are dealing with a peculiar form of the streptococcus.

Dr. J. William White, to whom the case was referred on account of the suspicion of syphilis, made the following report:

"The patient in question came to me on December 4, 1905. At that time he had a small papular, punctate, miliary eruption, irregularly grouped, profuse on the trunk, slight on the limbs. There was occasional itching. The inguinal, axillary, cervical, and supraclavicular group of lymph nodes were all enlarged. He gave me the following history:

"He had been well up to June, 1905. He then had urticaria lasting for three months, and very profuse. During this time he lost weight noticeably. In September his general health was poor but he had no local symptoms. In October, after drinking much mineral spring water, his general health improved, due, he thought, to the eliminative action of the fluid that he took in such large quantities, but toward the end of the month he had a heavy rigor, followed with fever (100° to 102°) and sweating, followed at once by palpable enlargement of the axillary lymph nodes and by sternal and substernal pain. After this a macular rash appeared, and his general condition became worse. The sternal pain extended; the sweats were profuse; there was marked dyspnœa; and about the end of October a distinct leukocytosis (21,000) was noted.

"He gave no history of any form of primary sore, or of any lesion, dry or ulcerative, that remotely resembled a chancre."

My expressed opinion was that he was suffering from some unusual form of toxemia, probably of tonsillar or gastrointestinal origin, and associated with a certain degree of toxic neuritis. I was then told of a slight development of jaundice that had accompanied his early symptoms, and of the appearance at about the same time of an eruption of an eczematous type which had affected the back, elbows, buttocks, and the posterior surfaces of the thighs. Still later, I learned that an examination of the blood, made at Dr. Stengel's request, had shown the presence of streptococci, and that the same organism had been found in cultures taken from the tonsils; all of which was, of course, evidence strongly confirmatory of the opinion I had given.

"Apart from the improbability that an intelligent, well-trained, and obviously intensely interested medical man would overlook or deny the existence of an initial lesion, and the comparative rarity with which such lesions remain undiscovered in the male, I was satisfied that the character and distribution of the eruption; the "intense" itching said to have been associated with certain of its early outbreaks; the urticarial character indicating a degree of nerve irritation unusual in syphilis, but in this case noticeable throughout (as a welt, bright red in color, could always be raised by slight friction of the skin); the degree of the fever and of the leukocytosis; the unusual enlargement of the lymph nodes (which much exceeded in size that of typical syphilitic glands); the direct associations of the symptoms with tonsillar and gastrointestinal phenomena, which seemed to indicate the probable channels of infection; the severity of the sternal, substernal, and general thoracic pain, easily explainable by an enlargement of the mediastinal nodes, comparable to that noticed in those that were more superficial and palpable, but most unusual in syphilis; all led me to believe that the theory above mentioned was probably correct. At any rate, I was quite unwilling to join in a diagnosis of syphilis or to give my approval to any anti-syphilitic treatment which could only confuse the diagnosis or perhaps make a positive diagnosis impossible.

"I next saw the patient on May 27, 1906, and found that in the interval the eruption had largely faded, but without the development of any deeper lesions, the formation of scales, the occurrence of mucous patches, or the appearance of alopecia. In other words, the intervening period was thoroughly atypical as regarded from the syphilitic standpoint. Furthermore, he reported to me that he had had several mild attacks of tonsillitis, on each of which occasions the eruption grew worse, and this was followed by the occurrence of articular pains jumping from joint to joint, and sometimes

severe enough to be quite troublesome. His leukocytosis in the meantime had dropped to from 8000 to 10,000. This seemed to me to warrant persistence in my original opinion, which at this date (May 11th) I still hold."

Dr. Henry W. Stelwagon saw the patient several times prior to and after our connection with the case and has kindly given us an account of his observations:

"When I first saw the eruption about November 1st, it had already lasted about one or two weeks. It consisted of discrete but rather numerous rosy-red macules, with but slight, if any, elevation; the color was not a bright red, nor could it be said to be dull. The eruption could be seen over trunk, upper parts of the arms and upper parts of the legs, but was for the most part upon the trunk. The lesions increased in number for a week or more, and then began to show in their central portions the development of pin-point to a pin-head sized papules, which finally increased slightly in size, but the papule was never as large as a small pea, holding mostly to the size of a medium-sized pin-head. The papule was of the same color as the macule upon which it developed. Some new macules continued to appear and some of the older lesions became less distinct, and probably some disappeared. There was, however, no capriciousness, as there was more or less persistence in all lesions; but there was a variable amount of change in their depth of coloring, the eruption as a whole being much more hyperæmic or red some times than at other times. There was no marked crowding together nor grouping of the macules. At this time there was no scaliness, but later the small papules were here and there capped with a minute scale. Upon pressure the new lesions seemed to disappear entirely, the older ones left a slight stain. Before the central papulation took place, the eruption was strongly suggestive of a macular syphiloderm, but the lesions were of a much brighter tint than was to be expected in this eruption, and could have been well considered as possibly a toxic macular erythema; but the individual lesions were much more persistent than one would expect in the latter rash. About the same time that the central papulation was developing, some macules appeared upon the forehead, and some upon the chin, and some near the nose and near the mouth, and later some of these showed slight scaliness, suggesting a patchy seborrhœa. Later, probably about three to four weeks after my first seeing the eruption, new small papules began to form in the neighborhood of the other papules, especially here and there in places, and the eruption became of a sluggish hue with a brownish tinge. When this condition had fully developed, the eruption consisted of some scattered macules, many with central papulation and irregular groups of brownish-red papules, the whole suggestive of a macular syphiloderm which had developed into an ill-defined and abortive miliary papular syphiloderm. As before, the rash showed some variation in its hyperæmic tinge from day to day, on some days being of a much brighter hue and of a puzzling character—too bright in hue for a syphilide; on other days, when the hyperæmic element was less marked, the diagnosis of a syphilide seemed the only permissible one. The eruption thus persisted with slight fluctuation for three or four months, gradually disappearing, having lasted in all about four to five months. The patient had a rather irritable skin and red lines and streaks could be easily provoked by rubbing, and it was due to this irritability of the skin, as it seems to me, that the eruption varied in its depth and brightness of coloring from time to time. There could scarcely be said to have been any distinct subjective symptoms."

In view of the confessedly atypical character of the eruption, the complete absence of syphilitic history and the negative result of the clinical examinations our thoughts were directed to other possible explanations of the curious clinical picture and especially the cutaneous and glandular features. From the beginning there was a strong presumption of some form of toxic or infectious disease and, in view of the long continuance of the symptoms, more decidedly that of an infection. The onset with gastrointestinal symptoms and tonsillitis, chills, and jaundice, and the successive development of fever, a skin eruption and glandular enlargement, of vague general pains and more localized pains under the sternum and in the joints all suggest a systemic infection. The occurrence of leukocytosis and anemia strongly corroborates this view and the bacteriologic examination confirmed it, though not in itself wholly excluding the possibility of another infection, such as syphilis, not certainly demonstrable to cultural methods.

It must, of course, be admitted that practically all of the symptoms referred to may occur in the early stages of syphilis. Thus the repetition of tonsillitis, the development of early jaundice, the appearance and persistence of fever, the recurring eruption in the skin and the pains and leukocytosis, all are possible manifestations of syphilis, but it is noteworthy that each of these occurred in a manner or degree quite unusual in syphilis. Placing those facts alongside of the denial of venereal or other syphilitic infection and the positive and identical results of culture from the tonsils and blood on several widely separated occasions the presumption seems to us a very strong one that the whole condition was one due to a form of streptococcus infection of unusual character.

The presence in the tonsils and in the blood on two occasions separated by one or two months of a streptococcus of peculiar character and properties establishes the existence of such an infection. The organism was certainly not of the pyogenes group and differed both culturally and morphologically from any of the streptococci usually encountered in human pathology. Though not in every respect identical with the descriptions of the Streptococcus equi found by Schütz and others in epidemic coryza and glandular enlargement of horses, the correspondence was suggestive.

The association of cutaneous lesions with mild or severe forms of septicopyæmia and with rheumatic polyarthritis has been recognized for a long time. The so-called surgical scarlatina (Thomas, Riedinger) is a simple form of this condition. It may present itself as an ordinary erythema or an erythema associated with urticaria and vesicles (Gussenbauer). Brunner has recently called attention to this condition and determined its relation to streptococcus infection. In a series of thirty-five cases of septic infection Litten found skin lesions in 80 per cent. Among the manifestations were multiple hemorrhages, jaundice, macular erythema, pemphigoid lesions, scarlatinous and morbilliform erythema with urticaria, hemorrhagic vesicles, hemorrhagic herpes, phlegmons, and erysipelas. Leube described herpes, hemorrhagic vesicles, and urticaria as associate cutaneous manifestations of cryptogenetic septicæmia. Deenig reports the dermal lesions of sepsis as of the type of erythema multiforme.

Kaposi, in calling the attention to the association of joint manifestations with erythema multiforme, suggests that this relationship suggests an etiological kinship or identity. A similar view has been put forward by Sir Dyce Duckworth, Smith, and other English authors. Boeck, Fowler, Garrod, Stewart, and Lasegue have referred to the occurrence of erythema nodosum or multiforme, or rheumatism and endocarditis as consequences of tonsillitis, and Gerhardt, Osler, and Lewin have emphasized the association of erythema multiforme with endocarditis and other grave visceral lesions.

If, as we believe, our patient's illness was due to a peculiar form of streptococcic infection it is probable that the tonsils were the original seat of the infection and portal of entrance of the organisms. The early occurrence of distinct pharyngitis and tonsillitis and the subsequent repetition of attacks as well as the appearance of the tonsils strongly indicated a local condition of the throat as the course of the continuous infection. However, as this is a matter of uncertainty we have used the title cryptogenetic infection, though we are impressed with the probable tonsillar origin of the disease.

THE CHARACTER OF THE THROMBI AND NECROSES OF THE LIVER, PRODUCED BY THE INTRAVENOUS INJECTION OF ETHER; CYSTIC DILATATION OF THE CAPILLARIES OF THE LIVER AS A RESULT OF INTRAVENOUS INJECTION OF ETHER.

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In regard to the action of ether after intravenous injection we find very contradictory statements in literature. Naunyn[1] believed he produced typical coagulation of the blood by injections of ether into the mesenteric veins of animals. Hanau[2] later states that he was able to produce white thrombi in the heart through injections of ether into the ear veins of rabbits. Aschoff[3] states that the ether does not produce any true clotting, but merely an albuminous precipitate. Flexner[4] in a study on agglutination thrombi says that by the injection of ether into the ear veins of rabbits he finds on opening the heart that the right side is filled with a dark, soft, agglutinated clot extending into the pulmonary vessels. Sections of the clot show part of the corpuscles in a state of shadows and others to be agglutinated; fibrin he notes as absent. Poisons which destroy the blood corpuscles are provocative of agglutination thrombosis. Ribbert[1] in his recent study on regeneration of the liver following artificially produced necroses did not find any thromboses as the result of the injection of ether into the mesenteric veins. As is well known, the injection of ether into a mesenteric vein is followed by necrosis of the liver. I have not been able to find any accurate statement in regard to the distribution of the necroses, at least in so far as literature has been accessible to me. Ribbert[2] states that necrosis may be found in all parts of the liver after injection of ether and that no regularity exists in this regard.

The following experiments represent a step in a series of researches into the factors underlying thrombosis. In former investigations I have found that the primary factor leading to thrombosis after injury of the bloodvessel wall consists in an agglutination of certain cellular elements of the blood; such an agglutination occurs also in the blood outside the body. Under these conditions no formation of fibrin needs

[1] Untersuchungen über Blutgerinnung im lebenden Thiere and ihre Folgen. Arch. f. exper. Pathol. u. Pharmacol., 1873, Band i.

[2] D. Entstehung u. Zusammensetzung d. Thromben. Vorl. Mitteilung, Fortschritte d. Medizin, 1886, Band iv.

[3] Ueber d. Aufbau. d. menschlichen Thromben u. d. Vorkommen von Plättchen in d. blutbildenden Organen. Virch. Archiv., 1892, vol. cxxx.

[4] On Thrombi Composed of Agglutinated Red Blood Corpuscles. Preliminary communication, Jour. of Med. Research, 1902, vol. viii.

[1] Z. Regeneration d. Leber u. Niere. Arch. f. Entwickelungsmechanik, 1904, vol. xviii.

[2] Vergleichende Untersuchungen über die Thrombose. Virchow's Archiv., 1906, Band clxxxv.

to take place. This agglutination is, as my investigations seem to indicate, found in all classes of animals and represents the original process by which bleeding to death after injury was prevented. Only in higher developed animals a coagulation process was secondarily added to the agglutinative phenomena.

In the present investigations I tried to analyze the conditions producing thrombosis by the injection of a certain substance leading to changes of the constitution of the blood by means of alterations of its cellular elements. I have used for this purpose ether. Besides thrombosis, the development of the necroses in the liver which follow injection of ether into mesentric veins, their possible dependence on a preceding thrombotic occlusion of the bloodvessels of the liver, and some mechanical effects of the injection of ether were studied.

In one series of experiments various quantities of ether were injected into the ear veins of rabbits and the effect of the injections on the blood and liver was studied. In a second series the blood was made incoagulable by injection of leech extract before the injection of ether in order to determine in this way whether or not ether causes a real intravascular coagulation of the blood.

In a third series the injections were carried out through the mesenteric veins instead of through the ear veins. In this way it was intended to decide how far the effects of the ether on the blood and the organs are local.

In a fourth series the injections of ether into the mesenteric vein were preceded by an injection of hirudin, in order to determine whether the parenchymatous lesions depend on the formation of fibrin thrombi.

Observations were made on the structure of cells in normal livers and in livers in which necroses had been produced.

In a fifth series pieces of liver of the same animals were excised before and after injection of ether in order to determine in a more exact way the influence of the effect of ether on the bloodvessels and parenchyma of the liver.

In a sixth series carmine was injected after the injection of ether or of ether and hirudin with the hope of determining the condition of the circulation after the injection of ether.

In a seventh series bloodvessels of the liver were clamped after injection of ether in order to determine the influence of the circulation on the origin of the necroses of the liver.

In a last series the injection of the ether was preceded by injection of adrenalin in order to investigate whether a contraction of the bloodvessels modifies the effect of the injection of ether. Further experiments in this and in other directions are planned.

INJECTION OF ETHER INTO THE EAR VEIN OR INTO THE JUGULAR VEIN OF RABBITS.

Ether was injected into seventeen rabbits, either through the ear vein or through the jugular vein. The amount varied from 0.75 c.c. to 10 c.c. In most cases the heart and the large vessels were examined inside the next five or six minutes. In a few cases the animals were killed twenty-four minutes, one hour and twenty-two hours later. Smaller amounts of ether (0.75 c.c., 1 c.c., 1.75 c.c.) did not cause intravascular clotting which was visible to the naked eye, provided the injection was carried out slowly. 1 c.c. ether could, however, produce clotting of the jugular vein, if the ether was injected rapidly. 2 c.c. and larger amounts of ether caused a coagulation of the blood in the heart and in the larger bloodvessels. Fresh pieces of clot examined microscopically showed very distinctly the presence of fibrin. In each case the thrombi found were red thrombi, consisting of fibrin with the inclusion of blood cells. In no case were white thrombi found in the heart.

In seven animals the livers and other organs were examined microscopically after injection of ether into the ear vein or into the jugular vein.

After injection of 1 c.c. and 1.75 c.c. ether into the ear veins of two animals no thromboses or necroses were found in the liver twenty-four hours later.

In another rabbit 1 c.c. ether was injected into the ear vein, and one hour later this injection was repeated. One hour and ten minutes later no thrombi and no necroses were found in liver. One hour and ten minutes after injection of 0.75 c.c.; twenty-two and one quarter hours after injection of 1. c.c. ether, no thrombi and no necroses were found in the liver.

In another case half-hour to one hour after injection of 1 c.c. ether into an ear vein, no necroses or thrombi were found in the liver.

A little more than 8 c.c. ether were injected into the ear vein of a rabbit; the animal died at the end of the injection; in the heart and in the abdominal vessels the blood was found to be clotted. In the large sublobular and central veins of the liver fibrinous clots were found, which had retracted and extended into some smaller veins. Not all of the vessels were clotted.

We see, therefore, that injection of a moderate amount of ether into the ear veins does not cause thrombi or thromboses in the liver. Injections of a large amount of ether may, however, cause thrombosis in the smaller branches of the liver veins very soon after the injection.

As a control, three rabbits were killed by a blow in the neck without a previous injection of ether. In one animal three minutes after death and in another twelve minutes after death no coagula were found in heart or vena cave; in a third case, six minutes after death some coagulum was found in the right auricle, a slight coagulum in the right ventricle, and a trace in the vena cava inferior. The cause of the coagulation in the last case is hard to determine. We can, however, be certain that the intravenous injection of ether caused the clotting in the experiments recorded above.

INJECTION OF ETHER INTO THE EAR OR JUGULAR VEIN PRECEDED BY AN INTRAVENOUS INJECTION OF HIRUDIN.

In order to determine whether the thrombi formed under the influence of an intravenous injection of ether were caused by the production of fibrin and were therefore caused by coagulative processes, or whether we had to deal with an agglutination of red blood corpuscles without the formation of fibrin, solutions of hirudin were injected previous to the injection of ether. Hirudin prevents or delays the coagulation of the blood without having any specific influence upon the agglutination of red blood corpuscles.

In six rabbits, 7 to 10 c.c. of a hirudin solution were injected into the ear or jugular vein; a few minutes later variable amounts of ether (2 c.c. to 10 c.c.) were injected into the ear or jugular vein. The heart and the larger blood-vessels of the animals were examined soon afterward (the periods varying in the different experiments from two to three minutes to fourteen minutes). The blood in the blood-vessels was always found to be uncoagulated. One experiment was especially interesting. 7 c.c. hirudin and soon afterward 9 c.c. ether were injected into the jugular veins. The animal died before the injection of ether was finished. Two minutes later the organs were taken out for microscopic examination. The central veins and many of the capillaries in the central part of the lobules of the liver were very much dilated. Some capillaries were so much dilated that small cysts were formed which compressed the surrounding rows of liver cells; no capillary spaces could be seen between such compressed rows of liver cells. The liver cells were at some places much drawn out; at other places the liver cells were torn from each other and hemorrhages had taken place. Undoubtedly we have here to deal with the effect of the ether—a large quantity of which had been rapidly injected into the jugular vein—becoming gaseous. The ether in its gaseous state distended the capillaries of the liver, compressed the rows of liver cells and separated the cells at other places. The substance of the liver cells and of the capillaries of the liver is sufficiently pliable to permit the formation of cysts under such conditions.

In another case in which the ether was injected into the ear vein without a preceding injection of hirudin no well-formed cysts were found. The coagulation of the blood taking place under the influence of the ether prevented probably the rapid entrance of large quantities of ether into the central veins of the liver. No microscopic examination of the liver of the other rabbits was made.

Injection of hirudin prevents the intravascular clotting after intravenous injection of ether. Some observations, however, indicate that an intravenous injection of ether shortens the time during which hirudin blood after having been withdrawn from the animal remains uncoagulated in vitro. The possibility that hirudin does not only prevent the clotting of the blood but that it prevents or delays equally well an agglutination of the erythrocytes had still to be considered. Several experiments were carried out to test whether addition of hirudin delays markedly the agglutination of red corpuscles which takes place under the influence of ricin.

In order to get conditions resembling as much as possible those existing inside the bloodvessels, in one experiment fresh undefibrinated blood of the rabbit was received through a cannula in test tubes containing hirudin and ricin solutions, and in other control tests tubes a 0.85 per cent. NaCl solution and ricin.

0.1 gram ricin was dissolved in 10 c.c. of a 10 per cent NaCl solution; 0.05 gram hirudin was disolved in 10 c.c.; 0.85 per cent. NaCl solution.

(*a*) 1 c.c. hirudin solution plus 1 c.c. ricin solution plus 3 c.c. rabbit blood.

(*b*) 1 c.c. 0.85 per cent. NaCl solution plus 1 c.c. ricin solution plus 3 c. c. rabbit blood.

(*c*) 1 c.c. hirudin solution plus 1.5 c.c. ricin solution plus 2.5 c.c. rabbit blood.

(*d*) 1 c.c. 0.85 per cent. NaCl solution plus 1.5 c.c. ricin solution plus 2.5 c.c. rabbit blood.

Agglutination begins after two minutes. (*a*) and (*b*) were one-third clear after twelve minutes; (*c*) and (*d*) were one-eighth clear at that time. After twenty-five minutes agglutination progresses in (*c*) and (*d*) much less than in (*a*) and (*b*).

After twenty-five minutes the test tubes are shaken up. After fifty-two minutes more erythrocytes are agglutinated at the bottom of the test tubes in (*a*) and (*c*) than in (*b*) and (*d*). Leech extract certainly has no noteworthy inhibiting effects upon the agglutination of erythrocytes which takes place under the influence of ricin.

INJECTION OF ETHER INTO A MESENTERIC VEIN OF A RABBIT.

Injection of ether into the ear vein or into the jugular vein causes intravascular clotting, which is visible to the naked eye provided the injection takes place rapidly or a large quantity is injected. In order to study the effect of slow injection of smaller amounts of ether, 0.5 to 2 c.c. ether were injected in most cases in about one-and-one-half to three minutes into mesenteric veins of twenty-one rabbits. Different parts of the liver of each animal were examined microscopically; usually, sections of other organs being studied simultaneously. These experiments afforded also an opportunity of deciding whether the effect of ether depends on the place of injection.

In the following a brief review of the main facts found in the different cases will be given. The different experiments are arranged according to time elapsing between the injection of ether and the excision of the liver for microscopic examination. The weight of the rabbits varied between 1500 and 2000 grams. Occasionally a heavier animal was used.[1] (Exact records of the weight of the different animals were kept in most cases.)

(1) 2 c.c. ether injected in two minutes and forty-five seconds; animal died about forty-five seconds after injection. Clot in portal vein and in right side of heart. Microscopically; thrombi in large portal veins; fibrin present in some, but not in all of the smaller portal veins. Fibrin can also be seen in a central vein; no necroses.

(2) 0.75 c.c. ether injected in mesenteric vein in one minute and forty-five seconds. Animal died two minutes after injection. Liver found hyperæmic; no macroscopic clot or necroses. Microscopically, no necroses; presence of fibrin in bloodvessels uncertain.

(3) 0.75 c.c. ether injected in one minute and thirty seconds; killed after five minutes; no macroscopic clot. Microscopically, no necroses; fibers (probably fibrin) present in some large and small portal veins.

(4) 1 c.c. ether injected in one minute and five seconds; killed after six minutes; no macroscopic clot. Microscopically, clots in portal veins and in neighboring capillaries, not in central veins. In areas in which thrombi were found, liver cells were somewhat changed, their nuclei were pyknotic, and the cytoplasm stained lighter.

(5) 1 c.c. ether injected in three minutes and thirty seconds; animal died ten minutes after the end of injection. Macroscopically, no clot. Microscopically, no clot, no necroses.

(6) 0.75 c.c. ether injected in two minutes and ten seconds. Killed twelve minutes later. Macroscopically, no clot; hyperæmia of liver. Microscopically no necroses, capillaries dilated; fibrin thrombi in portal veins.

(7) 0.75 c.c. ether injected in three mesenteric veins in one minute; killed after half hour. Macroscopically, no clot. Microscopically, no necroses; retracted clots present in some portal vessels and fibrin visible in some capillaries.

(8) 0.75 c.c. ether injected in two minutes and thirty seconds. Killed after one hour. Microscopically, no coagula in large vessels, but coagula in small vessels. Microscopically, retracted clots in portal vessels of different sizes; doubtful whether thrombi in central veins. Possibly beginning of a microscopic necrosis around a portal vein.

(9) 1 c.c. ether injected. Killed after one and one quarter hours. Macroscopically, no marked change. Microscopically, thrombi in a few portal veins; small periportal necroses.

(10) 0.75 c.c. ether injected. Killed after one and one half hours. Microscopically, no necroses, probably fibrin in a few large portal veins.

(11) 0.5 c.c. ether injected in one minute and twenty seconds; killed after four hours and twenty-five minutes. Macroscopically, necroses of liver. Microscopically, necroses around portal vessels and some hemorrhagic areas in liver. In many portal vessels fibrin thrombi, retracted fibrin-thrombi visible.

(12) 0.75 c.c. ether injected in one minute. Killed seven hours later. Necroses, hemorrhagic areas in liver. No clot in large vessels. Microscopically, large necroses, partly hemorrhagic, in liver; fibrin thrombi in portal veins, especially in necrotic areas, in some small portal vessels hyaline masses. Occasionally thrombi in central veins.

(13) 0.75 c.c. ether injected in two minutes and ten seconds. Animal died during the following night, probably ten to fourteen hours after injection, was examined the morning following death. Large vessels contain clots; coagula in liver vessels; large necroses in liver. Microscopically, large portal veins contain retracted clots. In some lobes of the liver the greater part of the liver tissue necrotic.

(14) 0.75 c.c. ether injected in two minutes and twenty seconds. Killed after eighteen hours. Macroscopically, necroses of the liver, small vessels of liver clotted; no clot in portal vein. Microscopically, in branches of portal vein fibrin present, periportal necroses in liver.

(15) 0.5 c.c. ether injected in one minute and fifty seconds. Killed after twenty-three hours. Necrotic and hyperæmic areas in liver; large vessels not changed; vessels in liver thrombosed. Microscopically, retracted clots in portal veins. Large necroses may extend to the areas around the central veins. Central veins dilated.

(16) 1 c.c. ether injected in three and one-half minutes. Killed after twenty-four hours. Necroses in liver. Microscopically, some hemorrhagic areas with fibrosis; large necroses; retracted thrombi in portal veins.

(17) 0.75 c.c. ether injected in about twenty-six seconds; died after four days (death probably caused by necrosis of part of the intestines as a result of ligature of a large mesenteric vessel). Right part of liver mostly necrotic, left part mostly normal. Macroscopically, thrombi in process of organization in many portal vessels; extensive necroses in liver; regeneration.

(18) 0.75 c.c. ether injected in one minute and thirty-five seconds. Killed after five days. Liver shows mottled appearance (gray and brown-colored areas); one hemorrhagic area. Microscopically, necroses and regeneration. In portal vein thrombus in process of organization.

(19) 1 c.c. ether injected in two mesenteric veins in two minutes and twenty seconds. Killed after fourteen days. Gray and brown areas in liver. Microscopically, necrotic

[1] If not stated otherwise, the organs were taken out immediately after death.

areas of liver surrounded by connective tissue. Regeneration in liver, in some portal veins thrombi in process of organization.

(20) 1 c.c. ether injected in three mesenteric veins in two minutes. Killed after four weeks. Large whitish areas in liver. Microscopically, no necroses; no thrombi; regeneration.

(21) 0.75 c.c. ether injected in fifty seconds. Killed after six weeks (animal gained in weight). Microscopically, in portal vein thrombus in process of organization; regeneration; no necroses visible.

From the preceding abstract it follows that microscopically the beginning of a necrosis could be approximately seen one hour after the injection of ether. Several small periportal necroses were present one and one quarter hours after injection of ether. In one case no necrosis could be seen one and one half hours after injection; more than two hours after injection of ether, up to two weeks after injection of ether, necroses were present in every case. Four weeks and six weeks afterward only regenerative processes were visible, the necrotic areas having been reabsorbed. The first necroses are therefore only microscopically visible, and appeared in this series first about one hour after injection of ether. They could be absent as late as one and one-half hours after the injection.[1] Later than one and one-half hours necroses were constantly present, they extended in size and became visible to the naked eye. The situation of these necroses was in each instance in the beginning typically periportal; they could extend deeper into the lobules and in some cases reached the central veins. Frequently the neighborhood of the larger portal veins was intact, and the necroses began around the smaller branches. The connective tissue surrounding the large portal veins had in all probability a protective influence. The slowing of the blood flow in the smaller vessels is probably also of importance in this connection. But it is nevertheless not rare to see the liver cells directly surrounding the large portal veins necrotic and even wide areas around the large portal veins can become necrotic. The bile ducts and the walls of the larger vessels with the surrounding connective tissue usually escaped necrosis; but there are cases in which bile ducts as well as the walls of the larger bloodvessels and the surrounding connective tissue became necrotic. The walls of the capillaries in the necrotic areas became usually necrotic. The changes in the necrotic liver cells consist in some cases in shrinking of the cells and nuclei; the cytoplasm stains relatively more with eosin. Sometimes cells with pyknotic nuclei are seen in the periphery of necrotic areas. In certain areas the cells are not markedly shrunken, the cytoplasm takes up very little stain, a disintegration and a solution of the protoplasm takes place, and only a few fibers remain indicating the outlines and situation of the liver cells.

The nucleus disappeared in the following way: the chromatin formed little globules or droplets which could either be distributed over the whole necrotic cell or were limited to the place of the former nucleus. The extent of this droplet formation was different in various cases and a sharp demarcation between karyorrhetic and karyolytic dissolution of the nuclei did not seem to exist. Leukocytes began to collect in the necrotic capillaries at a very early stage. They were seen in most necrotic areas; their number varied greatly in different places of the same liver. They were first seen in the necrotic capillaries, but penetrated later into the necrotic liver cells. In some instances their number became so great that small abscesses were formed. They frequently formed little agglutinated masses in the capillaries of the necrotic area; such masses might be spoken of as leukocytic thrombi which, if they did not entirely occlude the capillaries, at least formed marked impediments to the circulation in the necrotic areas. Many leukocytes could frequently be seen in the portal veins. At later stages leukocytes can be seen to degenerate, *e.g.*, twenty-three hours after injection of ether, degenerating leukocytes were seen in thrombosed vessels, and four days after injection in necrotic capillaries.

In four cases more or less extensive hemorrhagic areas could be seen in the liver; in one case in which the injection had been carried out rapidly (in one minute) a laceration of the walls of the larger portal vessels and hemorrhagic infiltration of some vessel walls had taken place.

In all cases fibrin thrombi were found in the portal vessels with exception of Cases 2, 3, and 10, in which the presence of fibrin was not certain. In two cases (Cases 1 and 13) macroscopic clots were found in the large vessels. In one of these two cases (Case 1) the largest amount of ether, namely 2 c.c., had been injected into a mesenteric vein. In Case 13 the animal had been lying dead for some time before examination. The clotting may therefore have been a postmortem clot in this case. In several cases the large vessels were free, but clots already visible to the naked eye were found in vessels of the liver on the cut surface. Such clots were seen in Cases 8, 13, 14, and 15, that is not earlier than one hour after injection of ether. In other cases thrombi were found on microscopic examination. Almost all clots were seen in the portal vessels. In Cases 1, 12, and 15 thrombi could also occasionally be seen in central veins. They were, however, not frequent. Whether in Case 8 thrombi were present in the central vein, is doubtful. These

[1] In one case (rabbit No. 4) certain microscopic changes in the periportal areas were already present six minutes after injection of ether. It is possible that in this case we had to deal with a very early effect of the ether, a relatively large quantity of which (1 c.c.) had been injected.

cases are those in which also in other respects the effect of the injection of ether was most marked, in so far as the clotting could already be seen by the naked eye: besides, the necroses were very extensive in Cases 12 and 15. The portal veins, however, were always principally affected and in most cases were the only ones containing clots. In several animals fibers of fibrin could be distinctly seen extending from a portal vein into adjoining capillaries. The fibrin fibers in thrombosed portal veins included occasionally many leukocytes of the blood in that part of the liver. Frequently the thrombi in the portal veins were fixed to the vessel wall and retracted toward the periphery of the vessel leaving the centre of the vessel open. Such retracted clots were seen as early as half an hour after the injection of the ether. Polynuclear leukocytes formed not rarely a marginal zone between the central lumen and the peripheral clot and in one case a second marginal zone of leukocytes could be seen in the periphery of the clots between the clot and vessel wall. This double layer of leukocytes can perhaps be interpreted in the following way: In the beginning there was a slowing of the blood current accompanied by the collection of leukocytes near the wall of the vessel. Coagulation took place and the peripherally arranged leukocytes were fixed in the meshes of the coagulum. The retraction of the clot followed soon and a slow circulation in the centre of the thrombosed vessel was again established with a collection of leukocytes in the periphery of the new road.

The fibres present in such clots stained with Weigert's fibrin stain. This stain, however, did not materially help to establish the presence of fibrin which could readily be detected by the ordinary hematoxylin-eosin stain. At many places there was undoubtedly fibrin present without any visible fibers. In such cases neither the hematoxylin-eosin nor the Weigert fibrin stain indicated the existence of fibrin, which surrounded the red blood corpuscles as a homogeneous mass. The distribution of the fibrin thrombi in the portal veins corresponds in the main to the distribution of the necroses. The thrombi are mainly found in the necrotic areas. We find however, not rarely, thrombi in portal vessels which are not surrounded by necrotic tissue; sometimes we can find under such conditions smaller thrombosed vessels, in the continuation of the larger vessels surrounded by necrotic areas; on the other side, we may find necrotic areas without being able to detect any distinct thrombi in the bloodvessels. The capillaries in the necrotic areas may, as stated above, occasionally contain fibers of fibrin; in other cases they may appear quite empty or a few red blood corpuscles or leukocytes are present. At other places many leukocytes can be seen in the capillaries. There are, however, two features which must be mentioned especially. It is not rare to see the capillaries in the necrotic areas filled with erythrocytes, often they are quite distended with red blood cells, more so than neighboring healthy capillaries. Sometimes the erythrocytes in the necrotic capillaries lose their hemoglobin, although the erythrocytes in the neighboring capillaries stain well with eosin and retain their hemoglobin. The outlines of those shadows of blood corpuscles are usually quite distinct. It is likely that a stasis occurs sometimes in the capillaries of the necrotic areas and substances are perhaps extracted from the surrounding necrotic tissue which gradually cause hemolysis of those impacted blood corpuscles.

Another observation which can be occasionally made is the following: A hyaline ring surrounds the central lumen of the capillaries; it appears as if the wall of the capillaries had been much thickened. This change is perhaps due to a swelling of the endothelial cells of the capillaries which afterward form a hyaline, homogeneous, necrotic mass. Whether this interpretation is correct, has yet to be determined by further investigation.

Hyaline or finely granular masses can be frequently seen in the portal veins as well as in central veins without any connection to necrosis of the surrounding tissue. These hyaline or granular masses represent plasma which became separated from the blood cells as a result of the difference in specific gravity and the separation probably takes place in the agone or postmortem. Occasionally, however, but not frequently, we see some hyaline masses staining red with eosin, which seem to be of a much denser consistency. They are found in smaller portal vessels. The character of these hyaline masses is not clear in this case. Possibly we have again to deal with coagulated blood plasma.

It is certain that the ordinary thrombi found in the portal veins after injection of ether are fibrin thrombi. They are formed during the life of the animal because not rarely they can be seen with the naked eye if a cut into the liver is made. Microscopically they are found as frequently at the margin as in the centre of the piece. Differences in fixation between the periphery and the centre of the liver pieces are therefore of no importance in this connection. Frequently the structure of the fibrin thrombi is such that a certain time was required for the retraction to take place. Moreover, at later periods, namely, after four and five days, after two and six weeks, thrombi could be seen in the process of connective tissue organization; this is a certain proof that those thrombi were formed during the life of the animals.

INJECTION OF ETHER INTO A MESENTERIC VEIN AFTER A PREVIOUS INJECTION OF HIRUDIN INTO THE MESENTERIC, JUGULAR OR EAR VEIN OF RABBITS.

After the effect of the intravenous injection of ether on the bloodvessels, on the blood, and the parenchyma of the liver had been studied and fibrin thrombi and necroses had been

found to occur, it was of interest to inject, previously to the injection of ether, hirudin into the bloodvessels, in order to prevent the intravenous clotting and separate if possible the action exerted by ether on the blood from its action on the parenchyma of the liver.

Twenty rabbits were used for these experiments. In each case the different parts of the liver and usually also of the principal organs were examined microscopically.

(1) 10 c.c. hirudin solution (0.05 gram) injected; four minutes later three-quarter c.c. ether in mesenteric vein. Animal died about one minute after injection. Blood does not coagulate. Microscopically, no necroses; no thrombi.

(2) 10 c.c. hirudin solution injected in jugular vein; three and one-half minutes later 1 c.c. ether in mesenteric vein. Animal died three minutes later. Blood does not coagulate. Microscopically, no necroses; no thrombi.

(3) 10 c.c. hirudin solution injected (0.06 gram hirudin) into ear vein; three minutes later 1 c.c. ether in mesenteric vein in one and three-quarter minutes. Killed after thirty minutes; blood still liquid the following day. Macroscopically, no changes. Microscopically, no thrombi; small periportal necroses present; dilated necrotic capillaries, either empty or filled with erythrocytes.

(4) 10 c.c. hirudin solution injected in jugular vein; four minutes later three-quarters c.c. ether in mesenteric vein. Killed after half an hour; blood does not coagulate; no thromboses; no necroses.

(5) 10 c.c. hirudin solution injected in jugular vein; one minute later nearly 1 c.c. ether in mesenteric vein; forty-three minutes later animal killed. Liver shows a few white necrotic spots to the naked eye; blood coagulation in vitro much delayed. Microscopically, no thromboses; small periportal necroses present.

(6) 8 c.c. hirudin injected in mesenteric vein, seven minutes later half c.c. ether in mesenteric vein. Animal dies from intraperitoneal hemorrhage one hour and fifteen minutes later. Blood coagulates very slowly in vitro. No macroscopic coagula in large bloodvessels and in liver no necroses. Microscopically only very few and small periportal necroses.

(7) 10 c.c hirudin solution injected in jugular vein; five minutes later three-quarters c.c. ether in mesenteric vein in one minute and forty-five seconds. One hour and ten minutes after the first hirudin injection inject 5 c.c. more hirudin in ear vein. Animal died twenty-five minutes after the last hirudin injection, one and one-half hours after ether injection. Liver cirrhotic; blood remains liquid. Microscopically, no fibrin thrombi. Thrombi of polynuclear leukocytes in capillaries in necrotic areas. Small and large periportal necroses; they may extend deeply into the lobule.

(8) 10 c.c. hirudin solution injected in ear vein; sixteen minutes later one-half c.c. ether in mesenteric vein. Animal died one and one-half hours after injection of ether. One hour later autopsy. Macroscopically, no change; blood found liquid. Microscopically, no thromboses; no marked necroses; a few isolated necrotic liver cells in periportal areas.

(9) 10 c.c. hirudin solution injected in jugular vein; ten minutes later inject three-quarters c.c. ether in mesenteric vein in one minute and forty seconds. Killed two hours later. Liver shows a few necrotic spots; blood remains liquid. Microscopically, no thrombi; some capillaries and small branches of portal vein filled with polynuclear leukocytes. Early stages of periportal necrosis.

(10) 8 c.c. hirudin solution injected in mesenteric vein in two minutes and twenty-five seconds; two and one-half minutes later inject two-thirds c.c. ether in mesenteric vein; died inside the next two and one-half hours. A few necrotic spots present in liver; blood remains liquid in vitro. Microscopically, no thromboses; a few periportal necroses. At one place a necrotic area shows hemorrhagic infiltration.

(11) 10 c.c. hirudin solution injected in mesenteric vein; ten minutes later two-thirds c.c. ether in mesenteric vein in two minutes; found dead after two and one-half hours; blood coagulates only a little in vitro. No macroscopic necroses. No microscopic examination.

(12) 9 c.c. hirudin solution injected in mesenteric vein; eleven minutes later three-quarters c.c. either in mesenteric vein in one and one-half minutes; died in convulsions two hours and thirty minutes later. A few necrotic areas in liver; blood coagulates in vitro very slowly. Microscopically, no thrombi present; cysts are formed in liver as a result of the injection of ether; periportal necroses in some parts of liver; necroses begun around medium-sized branches of portal vein.

(13) 9 c.c. hirudin solution injected in mesenteric vein; six minutes later three-quarters c.c. ether in mesenteric vein in one minute and thirty seconds. Killed three hours and thirty-five minutes later; a few whitish, necrotic spots in liver; blood coagulates in vitro loosely in five minutes. Microscopically no thromboses; small periportal necroses; some necrotic areas with hemorrhagic infiltration.

(14) 8.5 c.c. hirudin solution injected in jugular vein; eight minutes later three-quarters c.c. ether in mesenteric vein in two minutes and twenty seconds. Killed four hours later. Liver normal in parts, in other parts yellowish-gray necrotic areas. At margin of liver small hemorrhagic areas. Changes in liver distinct, but not so marked as in other cases. Coagulation of the blood in vitro not yet started after twenty-five minutes. After one hour very small coagula at bottom of dish. Microscopically, no fibrin thrombi; small periportal necroses.

(15) 8 c.c. hirudin solution injected in mesenteric vein; six minutes later three-quarters c.c. ether in mesenteric vein in one minute and twenty-five seconds. Killed four hours and twenty minutes later. Liver shows small gray-white necrotic dots, some parts of liver comparatively free from change

In contact with tissues one-half of the blood coagulated in vitro in ten minutes. Microscopically, periportal necroses with variable amounts of polymuclear leukocytes, occasionally forming small abscesses in the periphery of the necrotic areas. No fibrin thrombi; in a few portal veins in the necrotic areas hyaline masses, sometimes including leukocytes.

(16) 10 c.c. hirudin solution in mesenteric veins; seven minutes later three-quarters c.c. ether in mesenteric vein in two minutes and ten seconds. Killed after four hours and thirty-five minutes. Coagulation of blood in vitro delayed. Liver pale, only in one part small necrotic (white) dots found. Microscopically, very small periportal necroses with leukocytes in capillaries and sometimes in tissues; no fibrin thrombi (part of the ether had been rapidly injected).

(17) 10 c.c. hirudin solution in jugular vein; fifteen minutes later two-thirds c.c. ether in mesenteric vein in two minutes. Killed seven hours later. Blood coagulates very slowly in vitro. Liver very much changed; large and small necrotic gray areas at some places; at other places normal tissue. Microscopically large necroses, starting in portal areas, sometimes affecting a whole lobule. In one portal vein perhaps some fibrin visible, otherwise no thrombi. In necrotic capillaries shadows of red blood corpuscles.

(18) 9 c.c. hirudin solution in mesenteric vein; four minutes later three-quarters c.c. ether in mesenteric vein in one minute and fifty seconds; died nineteen hours later. Blood taken out fifteen minutes after death. Liver shows small yellowish-gray dots, at some places they are confluent. In such necrotic areas coagula visible in small vessels of the cut surface. Microscopically large periportal necroses; many leukocytes in capillaries and sometimes in liver cells of necrotic areas. In one portal vein fibrin distinctly visible; most vessels without fibrin.

(19) 10 c.c. hirudin solution in jugular vein; four minutes later nearly 1 c.c. ether in mesenteric vein in three minutes and thirty-five seconds. Killed after twenty-three hours. Blood coagulates somewhat more slowly than usually; liver contains many small yellow dots; very diffuse distribution of lesions; slight hemorrhagic areas in liver. Microscopically small and somewhat larger necrotic areas around portal veins; leukocytes in many necrotic capillaries; no hyaline thrombi; in a few portal veins possibly fibrin present.

(20) 8 c.c. hirudin solution in mesenteric vein; seventeen minutes later one drop ether in mesenteric vein; died between one and one-quarter and two and one-quarter hours later. Animal examined two and one-quarter hours after injection. Blood coagulation much delayed in vitro; after twenty minutes one-half of blood coagulated; no necroses. Microscopically, no necroses; no thromboses.

From these experiments it follows that a previous injection of leech extract does not prevent the necroses of the liver which are produced by ether. They appear at least as early as without the injection of hirudin. To the naked eye necroses become visible about two hours, but microscopically they begin to appear as early as thirty minutes after the injection of ether. They are not yet present in another specimen after thirty minutes; they can again be seen forty-three minutes and one hour and fifteen minutes after injection of ether.

From now on they are regularly present, but as late as one and one-half hours after injection they can be still very slight. Although the necroses appear at least just as rapidly after injection of hirudin and ether as after the injection of ether alone, the necrotic areas are much diminished in size and number in this series, in the first five hours after injection. At still later periods they may, however, be quite large. It is very probable that the previous injection of hirudin diminished the extent of the necroses. The same difference was found in later experiments in which simultaneously with the injection of ether alone or of ether and hirudin the liver vessels were occluded.

A second point of difference between the series of experiments with and without a previous injection of hirudin is that in the latter series fibrin thrombi could easily be seen in the large majority of cases; in the hirudin series on the other side, fibrin thrombi appeared for the first time seven hours after the operation, at which period the effect of the hirudin had to a great extent passed off; and even then these thrombi were only few in number. It must however, be emphasized that microscopically the presence of fibrin between blood cells cannot always be excluded with certainty, so that at later stages when the blood had regained its normal coagulability the possibility of the presence of some unrecognized fibrin thrombi cannot be entirely excluded. Such thrombi were certainly absent in the first stages.

Polymuclear leukocytes collect very early in the capillaries of the necrotic areas and they soon begin to penetrate into the necrotic liver cells. As early as forty-three minutes after injection of ether leukocytes can be seen to penetrate into necrotic liver cells. At all the later stages leukocytes can be seen in the necrotic capillaries as well as in the liver cells of the necrotic areas. Their number in different parts of the same liver is very different. Inside the capillaries perfect thrombi of agglutinated leukocytes can occasionally be found, as for instance one and one-half hours after injection of the ether. Leukocytes fill also, in other cases, the capillaries in such large numbers that a serious obstruction to the circulation must follow inevitably. The collection of the polymuclear leukocytes can become so large that small abscesses are formed in the periphery of the necrotic areas, for instance in rabbit 15 four hours and twenty minutes after injection of ether. It is very likely that the leukocytes contribute to the destruction of the necrotic liver cells, as frequently little of the cells and nuclear substance is left at

places where many leukocytes had previously collected. On the other hand, leukocytes are not necessary for the dissolution of the liver cells, which can take place without their presence. The necrotic changes in the walls of the capillary vessels and in the liver cells seem to be the primary process, which is frequently followed by a collection of leukocytes.

In regard to the morphological changes taking place in the necrotic liver cells it is of interest that at a very early period, as for instance thirty minutes after injection of the ether, the destruction of the liver cells can have progressed very far, in some of the cells only a bare outline being left, with some fibrils traversing the cell. Other cells, although necrotic, may be much better preserved. On becoming necrotic the nuclei may retain their size or they may shrink. The chromatin can be washed out from previously shrunken nuclei as well as from nuclei retaining their normal size The chromatin may form droplets or granules of different size; they may be enclosed by the nuclear membrane or the latter may become dissolved and the chromatin may or may not be dispersed over the whole cell. In regard to changes in the capillaries, the endothelial cells can become necrotic very early, as for instance two hours after injection of ether. The appearance of hyaline rings in the capillaries may perhaps be due to a swelling of the necrotic wall of the vessel. The necrotic capillaries are frequently dilated and may be filled with masses of erythrocytes which can be free from hemoglobin, although other erythrocytes stain well with eosin. Some stagnation seems to occur, which is perhaps due to the collection of leukocytes. The dilatation of the capillaries which connot rarely be observed may be caused by the decrease in the elasticity of the surrounding necrotic liver tissue. The hemolysis which takes place occasionally in blood corpuscles in necrotic areas is perhaps produced by substances which diffuse from the surrounding tissue through the necrotic wall into the capillaries and affect the red blood cells.

ON THE STRUCTURE OF THE HEALTHY LIVER CELLS BEFORE AND AFTER INJECTION OF ETHER.

In the large majority of cases the cells situated around the portal vessels in the liver of the rabbit have a denser, more homogeneous structure than the cells in the area of the central vein or in the zone between the central and the portal areas. This difference in structures manifests itself also in the fact that the denser cells assume a deeper blue stain with the hematoxylin; there are more granules present in the same space than in the other cells, which have a more vacuolar structure. Occasionally such dense cells are not only found in the portal areas but also in the central areas, the zone between these two areas alone containing vacuolar cells. It can also occur that all liver cells are almost equally vacuolar or that they are all of a homogeneous character. Even then the portal cells may show a still more homogeneous structure.

If we leave at present the necrotizing effect of the ether out of consideration, the injections of ether do not seem to cause any marked change in the structure of the liver cells. There is, however, one change noticeable which is not without interest. In case periportal necroses are produced it is quite a frequent occurrence that the cells directly surrounding the necrotic areas assume the properties which are otherwise characteristic of the now necrotic liver cells of the portal areas. It is possible that all these differences in the structure of the cells depend on the differences in the glycogen contents of cells in the various areas of the liver. That is a problem to be determined by further investigation.

EXCISION OF PIECES OF LIVER BEFORE AND ONE AND ONE-HALF TO FOUR HOURS AFTER INJECTION OF ETHER INTO A MESENTERIC VEIN. EFFECT OF THE INJECTION OF ETHER ON THE FAT CONTENTS OF THE LIVER.

In seven rabbits small pieces of liver were extirpated before the injection of ether; one and one-half to four hours after injection of three-quarters c.c. of ether into the mesenteric vein of the same rabbits pieces of liver were again cut out for microscopic examination. In the control pieces examined before injection of ether neither necroses nor thrombi in the bloodvessels were found; in the pieces taken out after the injection of ether necroses were found in each animal; they were situated in the periportal areas. In the early stages, one and one-half to two hours after injection, small necroses were found; four hours after the injection of ether large necroses could be found. One and one-half hours after the injection of ether the necroses were visible only microscopically; from one hour and fifty minutes on the necroses were already visible to the naked eye. After injection of ether fibrin thrombi were found in the portal veins. Occasionally such fibrin thrombi could be seen to extend into the capillaries which were running through the necrotic areas. At some places thrombi were present without necroses around the thrombosed vessels; generally, however, the distribution of the necroses corresponded in the main to the distribution of the thrombi. Pieces of the liver before and after injection of ether were fixed in formalin, sections were made with the freezing microtome and stained with Sudan III. The results obtained were briefly as follows:

Rabbit I. A little more fat was present in the pieces excised one and one-half hours after the injection of ether than in those examined before injection of ether.

Rabbit II. No marked difference in the fat contents of the pieces excised before and one and one-half hours after injection of ether.

Rabbit III. No fat could be seen in this liver before or two hours after injection of ether. (No fat visible in necrotic areas.)

Rabbit IV. More fat is present in the piece excised one hour and fifty minutes after injection of ether than before. There is some increase of fat in the areas of beginning necrosis.

Rabbit V. Approximately the same amount of fat present before and three hours and fifty-five minutes after injection of ether. The necrotic areas were free of fat; in the periphery of one necrotic area some fat could be seen.

Rabbit VI. No marked differences between pieces extirpated before or three hours and twenty minutes after injection of ether. In, or in the periphery of, the necrotic areas no, or only little, fat is found.

Rabbit VII. No fat found; no fat can be seen in the areas of beginning necroses.

From this abstract we see that, as far as Sudan III indicates, fat necroses caused by injection of ether do not need to be accompanied by any increase in the fat contents of the necrotic area, at least in the early stages of necrosis. Neither are the fat contents of the rest of the liver materially changed in the next few hours after the injection of the ether.

INJECTION OF ETHER INTO A MESENTERIC VEIN WITH AND WITHOUT A PRECEDING INTRAVENOUS INJECTION OF HIRUDIN. INJECTION OF CARMINE INTO THE PORTAL VEIN SHORTLY BEFORE THE DEATH OF THE ANIMAL.

In order to determine the permeability of the bloodvessel of the liver after injection of ether into a mesenteric vein an ammoniacal solution of carmine was injected into the portal veins of rabbits four to four and one-half hours after injection of the ether. Three rabbits were treated in this way. It was found that the carmine solution did not penetrate well into the necrotic areas. This was already visible to the naked eye and it was confirmed by microscopic sections of the injected liver. The capillaries of the healthy parts frequently contained particles of carmine; the capillaries of the necrotic areas were entirely free of it. In three other experiments the rabbits received before the injection of ether an injection of hirudin sufficiently large to prevent the coagulation of the blood for a certain period. In all three of these cases the same results were obtained. The carmine penetrated into the healthy capillaries but not into the necrotic areas. In one of these three rabbits no fibrin could be observed in the capillaries; leukocytes, however, were frequently present in large number and could be seen to occlude the vessels. In a second case small fibers could occasionally be seen in necrotic capillaries besides accumulations of leukocytes. These fibers may have been fibrin. In a third case besides small fibers hyaline ring-like masses were visible in some necrotic capillaries. These rings may perhaps have been formed by the swelling of the endothelial cells of the capillaries. In other cases shadows of red corpuscles filled those capillaries. At some places well-preserved erythrocytes were present. In all six animals periportal necroses were found. In those animals, however, which had received an injection of hirudin, the number of necroses was markedly smaller than in the three other rabbits.

The carmine solution caused frequently a diffuse red staining of some periportal areas. Simultaneously changes in some cells and swelling of nuclei were not rarely caused by the alkalinity of the solution. A number of necrotic areas, however, remained intact, and at such places it could be especially well seen that the capillaries of the necrotic areas remained free of certain particles.

The injections were made approximately four hours after the injection of hirudin. At that time the effect of the hirudin had to a great extent already disappeared. Besides leukocytic masses occluded frequently the capillaries. These conditions may perhaps explain the fact that the carmine did not penetrate into the bloodvessels even after a previous injection of hirudin. There may have been, however, still other circumstances at present unknown that produced this result.

INJECTION OF ETHER INTO A MESENTERIC VEIN FOLLOWED BY LIGATION OF PORTAL VESSELS.

In three rabbits a part or all of the portal vessels were ligated or clamped a few minutes after a previous injection of one-half to three-quarters c.c. ether into the mesenteric vein. Two animals died fifteen and forty-five minutes later, the third animal was killed after an interval of three and one-half hours. In all three cases fibrin coagula were found in the portal veins. Sometimes the coagula had contracted and plasma had been pressed out into the centre. Here again fibers of fibrin could be seen. In the rabbit killed, in three and one-half hours well-developed necroses were found; they originated in the periportal areas. In necrotic areas which were situated in those parts of the liver in which marked circulatory disturbances had taken place, distention of capillaries and veins as a result of the experimental occlusion of bloodvessels, but no leukocytes were found. In the other two rabbits which had been killed at a relatively early period only very slight or no necroses were present. In one of these rabbits small cysts had formed in the liver through distention of the capillaries; the rows of liver cells were compressed.

In two rabbits the bloodvessels of a part of the liver were ligated without a preceding injection of ether. These animals were killed three hours and three and one-half hours respectively after the operation. Here dilatation of veins and

capillaries and small necroses in the periportal areas were found. The cytolytic processes in the necrotic areas were quite marked, in as much as often merely the outlines of the cells remained, after a complete resorption of the nucleus and cytoplasm. No thromboses could be seen. Whether the circulatory disturbances were the cause of the relatively small number of necroses, has to be determined by further experiments.

INJECTIONS OF ETHER INTO A MESENTERIC VEIN AFTER A PRECEDING INTRAVENOUS INJECTION OF ADRENALIN.

Four rabbits were first injected in the ear vein with 0.1 c.c. of an adrenalin solution (1 to 1000, Parke-Davis preparation) and a few minutes (in one case fifteen minutes) later 0.5 to 0.75 c.c. ether were injected into a mesenteric vein. A fifth rabbit was injected with a 0.3 c.c. adrenalin solution into a mesenteric vein and three minutes later with 0.75 c.c. ether likewise into a mesenteric vein. This animal died five minutes after the injection of ether. As a result of the injection of ether a dilatation of several small portal veins had taken place and rows of liver cells were compressed; at some places a whorl-like arrangement of rows of liver cells was likewise caused by injection of ether. Many portal veins were thrombosed. In all of the four other rabbits fibrin thrombi were found in portal veins. Periportal necroses were present with varying numbers of polynuclear leukocytes in the capillaries and in the necrotic liver cells. At some necrotic places leukocytes could be entirely absent. In two of these four cases extensive hemorrhages were found, in one case the hemorrhages taking place in the necrotic area itself, in the other case the hemorrhagic areas were situated midway between the portal areas and the areas of the central vein, the hemorrhages thus surrounding the necrotic places. Such extensive hemorrhages were only found in these two rabbits which had received an injection of adrenalin as well as of ether, although a more limited hemorrhagic infiltration was occasionally found in other cases. The size of the necrotic areas varied in these rabbits.

These experiments were undertaken in order to determine whether the effects of the intravenous injection of ether could be increased by a constriction of the smaller bloodvessels caused by the previous injection of adrenalin.

SUMMARY.

1. Injections of small quantities of ether into the ear vein does not produce intravascular clotting visible to the naked eye. After injections of large amounts of ether into the ear vein or jugular vein fibrin thrombi are found in the heart and in large vessels, and on microscopic examination fibrin thrombi are found in some of the smaller liver veins. After injections of smaller quantities of ether into the ear veins no thrombi and no necroses are found in the liver. White thrombi are not produced through injection of ether into the ear or jugular veins.

2. The large thrombi which are formed under the influence of ether are typical fibrin thrombi. Fresh pieces examined under the microscope show the presence of fibers of fibrin. An intravenous injection of leech extract preliminary to the injection of ether prevents the formation of these thrombi entirely. An injection of ether after an injection of leech extract may, however, accelerate the coagulation in vitro of the leech extract blood. The very marked inhibiting action of the leech extract is a further strong proof of the fact that these thrombi are fibrin thrombi, and not albuminous precipitate or thrombi of agglutinated red blood corpuscles.

3. Hirudin does not have a markedly inhibiting effect upon the agglutination of erythrocytes taking place under the influence of ricin.

4. After injection of a large amount of ether into the jugular vein cysts may be produced in the liver through marked dilatation of some capillaries or of some small portal veins of the liver lobules. The rows of liver cells adjoining such cysts were compressed and drawn out. The dilatation was produced as a result of the evaporation of the ether at body temperature, the cysts formation probably was favored through a previous injection of hirudin which prevented intravascular clotting and enabled the ether to penetrate rapidly in large quantities into the liver. In another case in which no hirudin had been injected and an extensive intravascular clotting had taken place no such cysts were formed. Small cysts were likewise occasionally found in the liver in some other cases after injection of ether into a mesenteric vein. The soft concistency of the protoplasm of the liver cells is well demonstrated by means of this experiment.

5. After injection of ether into mesenteric veins fibrin thrombi are found in the large majority of cases in portal veins; they may extend into capillaries and occasionally into central veins. Besides the fibrin thrombi small leukocytic thrombi may be found in capillaries. The erythrocytes in necrotic areas may appear free of hemoglobin. The presence of hyaline thrombi formed through the agglutination of red blood corpuscles could not be found with any degree of certainty. If slightly larger amounts of ether were injected clots could be seen in the portal vessels by the naked eye. The fibrin thrombi were found very soon after injection of ether and were formed intra vitam.

6. As the result of the injection of ether, necroses were found in the liver. They originated in all cases around the portal vessels and usually around the smaller ones, the connective tissue surrounding the larger vessels apparently serving as a protective tissue against the destructive action of

the ether. The extent of the necrotic and histolytic changes is different in different cases; equally variable is the number of leukocytes present in the necrotic areas. On the whole pronounced necroses and thromboses coincided, but apparently not in every case. In this series necroses were visible microscopically as early as one hour after injection of ether, extended gradually in size and intensity and became visible to the naked eye a few hours later. They were still visible two weeks, and had disappeared four weeks after injection of ether. Occasionally, the necrotic areas can be more or less infiltrated with blood.

7. If the injection of ether into a mesenteric vein is preceded by an injection of hirudin no distinct fibrin thrombi can be seen in the portal vessels or capillaries in the next seven hours after the injection and they are not extensive at later stages. The necroses of the portal area of the liver are found nevertheless as early as half an hour after injection. They enlarge somewhat in size and become visible to the naked eye two hours after injection. They are, however, much smaller than without a previous injection of hirudin; they may somewhat enlarge at later periods. It is therefore probable that the ether causes necrosis of the liver cells directly and not only indirectly through the production or thrombi, because necroses are found without the presence of fibrin thrombi as early as half an hour after injection of ether. It is, however, possible that the thrombi contribute secondarily to the growth of the necroses, as after an hirudin injection the thrombi are much smaller in size and are present in smaller number. Other effects of hirudin by which the diminution of the necroses may be produced can, however, not yet be excluded. In regard to the morphological character of the necroses and in regard to the action of the leukocytes no distinct differences exist between this series and the former one, in which no hirudin was injected.

8. The cells of the normal liver of the rabbit show structural differences in the different areas of the liver. Injections of ether do not materially alter these structural characteristics. It is, however, a very frequent occurrence, that if the portal areas become necrotic the cells directly surrounding the portal areas assume the structural characteristics of the portal cells.

9. Necrosis caused by injection of ether does not need to be accompanied by an increase in the fat contents of the necrotic areas, at least in the early stages of the necrosis; neither are the fat contents of the rest of the liver materially changed in the next few hours after injection of ether. This holds good when the Sudan III is employed as a stain.

10. Four hours after injection of ether into mesenteric veins of a rabbit with or without a preceding injection of hirudin, the capillaries of the necrotic areas are not permeable to particles of carmine. The collection of leukocytes in the capillaries may cause an obstruction to the flow of blood. At this period the effect of hirudin has to a great extent subsided; the formation of fibrin thrombi in the necrotic areas can therefore not be excluded with certainty.

11. After injection of ether followed by experimental occlusion of bloodvessels of the liver a very marked formation of fibrin thrombi was found in the necrotic area. Under those conditions no leukocytic infiltration of the necrotic areas took place.

12. After a previous injection of adrenalin, injections of ether produced in several cases very extensive hemorrhages in the liver. The hemorrhagic areas coincided either with the necrotic foci, or the hemorrhages had taken place into a zone midway between the portal and central parts of the acini.

13. Of interest is the not infrequent appearance of hyaline rings in necrotic capillaries in the necrotic areas of the liver after injection of ether. They are probably caused by a hyaline swelling of the necrotic walls of the vessels.

14. We see therefore that intravenous injection of ether causes the production of fibrin thrombi. Ether acts by the destruction of cellular elements of the blood (red blood corpuscles, whether other cells are affected is uncertain). Substances are set free which convert fibrinogen into fibrin. These substances are in many respects similar to the tissue coagulins found in other cells, but it is by no means certain that they are identical with those substances. The formation of small leukocytic thrombi found sometimes after injection of ether is probably a secondary process following necrotic changes in the tissues. These necroses represent in part at least a direct action of the ether upon the tissues. Following the toxic action of ether upon the cells, autolytic changes take place in all probability and produce the morphological appearances described above.

THE NUCLEUS TEST IN PANCREATIC DISEASE.[1]

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(From the Clinical Laboratory of the Presbyterian Hospital in Philadelphia).

In a paper read before the Congress for Internal Medicine in 1904, Adolph Schmidt, of Dresden, suggested a new method of diagnosis in pancreatic disease, namely, the so-called nucleus test. Schmidt first demonstrated in artificial digestion experiments outside the body that the cell nuclei are digested by the secretion of the pancreas alone and are not affected by the other digestive ferments. He then devised the method of passing small pieces of meat through the gastrointestinal tract and examining them for nuclei after their recovery in the stool in order to determine the activity of the pancreas. One of Schmidt's pupils, Wallenfang, of Bonn, showed experimentally that when the pancreas of dogs is extirpated the nuclei of the meat fiber came through undigested. Wallenfang's experiments seemed to show that the lesion of the pancreas must be complete to produce this effect. In three dogs in which the pancreas was entirely removed the nuclei were never digested. In healthy control dogs they were always totally digested. In one dog in which a small piece of pancreatic tissue was unavoidably left in place the nuclei were all digested.

A series of clinical observations by Schmidt appeared to confirm these experiments. He reported tests upon 100 cases of healthy persons and patients with gastrointestinal disease not pancreatic in which the nuclei were always digested. His list included cases of cancer of the liver, closure of the bile ducts by stone, catarrhal swelling, achylia with diarrhœa, tuberculous and catarrhal enteritis, and colitis. Schmidt examined six cases of pancreatic disease, four with and two without autopsy. Two of the cases with autopsy were instances of incomplete lesion of the pancreas, and in the other two the pancreas was entirely destroyed or its duct absolutely closed so that its secretion was entirely cut off. In the first two cases of incomplete lesion the nuclei were completely digested. In the case of complete lesion the nuclei were not digested.

Hemmeter has also demonstrated the persistence of nuclei in meat after its passage through the gastrointestinal tract in a case of pancreatic cyst and in one of stenosis of the duct after cholelithiasis. Both patients recovered after operation and in a few weeks no nuclei were found indicating resumption of the pancreatic function. These observations of Hemmeter's as far as they go are more convincing than those of Schmidt, because they show that the digestion of the nuclei commenced again as soon as the obstruction to the pancreatic duct was removed. The technique of the test is as follows:

The meat must not be too long in passing. Schmidt has shown by experiments outside the body that in twenty-four hours the nuclei may be digested by the action of the intestinal bacteria. I can easily believe this although I have no direct evidence upon the matter except the nuclei are destroyed around the edge of meat-balls which were passed through the case of pancreatic disease, although the rest of the nuclei were not digested. I usually give the balls with the noon meal and then give laxatives if necessary to insure their recovery next morning, thus allowing about eighteen hours for their passage. When the meat is carried through too quickly the nuclei will not be digested, presumably because not enough time has been given for the proper action of the digestive juices. I have seen this repeatedly in my normal cases and in patients with diarrhœa. I agree with Schmidt that twelve to fourteen hours should be the minimum period, and I feel more certain if eighteen hours is allowed.

The meat-balls must not be larger than 0.5 cm. in diameter or about the size of a pea. They are cut from the round of beef, hardened in alcohol for a few days, then tied up in a little bag of Brussels net and kept in alcohol until used. The mesh of the net should be fairly large so that the balls can be easily discovered in the stool. A fine silk net, like veiling, is undesirable, as it becomes almost invisible when it is wet, and this makes the balls very hard to find. The stool should be examined promptly, best by mixing it with water and passing it through a sieve. No test should be considered positive unless practically all the nuclei remain intact in several examinations. In my experience the nuclei of the outer zone of the meat-ball are destroyed, in all cases, probably by bacterial action. In positive tests all the nuclei except this outer layer should remain intact. In normal cases there are almost always a few nuclei left at the centre of the ball, and often here and there throughout the microscopic sections there are patches of nuclei remaining. Therefore, I think that Schmidt is right when he makes the statement that a test must never be considered positive unless all the nuclei remain intact. Like so many methods of gastrointestinal diagnosis attempts

[1]Read before the Association of American Physicians, May, 1906.

to draw too fine distinctions will lead to error. We must be content to deal in round numbers and to consider no test positive unless it is decidedly so.

Schmidt says that the examination for nuclei can be made at once by testing the meat fiber in acetic acid. I am certain that not much reliance can be placed upon this method for the reason already given, namely, that often in normal cases some nuclei remain intact. Consequently, if we found nuclei in the examination of the teased specimen we could not be certain that the test was positive unless the whole ball was teased and examined. It is much better to imbed, cut, and stain the ball. This can readily be done by one of the modern methods of rapid imbedding, because the sections need not be very carefully prepared and should not take longer than a day or so.

My clinical experience with the nucleus test in two cases of demonstrated pancreatic disease and in nine others in which there was no clinical evidence of that condition does not entirely support Schmidt's claim for the method.

I say this for several reasons: First, because the nuclei resisted digestion in Case I, in which there was every reason to suppose that the pancreatic duct was not entirely occluded, although operation demonstrated considerable thickening and hardening of the organ itself. On the other hand, the nuclei regularly disappeared in the case of carcinoma in which several operations showed very extensive involvement of the pancreas and total occlusion of the common bile duct near its point of entrance with the duodenum. Moreover, the poor digestion and poor absorption of fats was much more pronounced in this case than in Case I. The stools showed neutral fat, a great excess of fatty acids, and an excess of soap. There seemed much more likelihood that the pancreatic duct was occluded in this patient than in Case I in which the nuclei persisted. Second, the nuclei resisted the digestion quite regularly in a case of complete achylia in which there was no disease of the bile ducts and no signs of pancreatic disease.

Our experiments with dogs in the Laboratory of Surgical Pathology, although carefully performed, did not give results at all similar to those of Schmidt and Wallenfang. A meat-ball of the size stipulated by Schmidt is usually completely fragmented by passage through a dog's digestive tract, and it is difficult to obtain pieces large enough to examine. Especially is this true in normal dogs and in those in which the pancreatic secretion is only partially cut off. When the pancreatic duct is ligated at its point of entrance into the duodenum, thus entirely precluding the entrance of pancreatic secretion into the intestine, the meat is not quite so completely digested, but even then it is so fragmented that all of the fibre must be exposed to the action of the intestinal bacteria to a much greater extent than when the meat-balls are passed through a human subject. In our dog experiments only once was there a piece of meat-ball passed large enough for satisfactory examination. This contained nuclei and was part of a meat-ball from a dog in which the pancreas was entirely tied off. When the meat-ball is so fragmented that the single fibers are separated, then the absence of their nuclei is of no significance since all of their nuclei must have been exposed to the action of the intestinal bacteria which is quite capable of destroying them. Thus it will be seen that as far as our work goes it confirms the observations of Wallenfang, but that it was not sufficiently satisfactory to be conclusive.

Our technique might be criticized in that we did not entirely extirpate the pancreas but tied off its duct, thus leaving room for error because there might have been some abnormal arrangement of the duct or accessory ducts. Thus the secretion would not have been entirely shut off. This criticism is deserved in some degree. However, at operation there seemed to be but one duct, and this was tied closely to the bowel. If any pancreatic secretion at all entered the intestine in the two dogs thus treated the amount must have been very small. However, Dr. Müller has now under observation a series of dogs in which the pancreas has been entirely extirpated, and later we hope to report the results of the nucleus test upon these dogs. In so far this paper must be considered a preliminary communication.

Finally, I wish to suggest that we may be wrong when we assume because of certain experiments in vitro that there is a specific relation between the digestion of certain tissue and certain digestive secretions. For example, Sahli, Schmidt, and others have asserted that raw connective tissue can only be digested in the stomach, and is not changed in the intestine. Sahli has based his so-called "desmoid test" upon this assumption, which is founded upon experiments performed outside the body.

However, Einhorn has lately shown quite conclusively, I think, that raw connective tissue can be digested in the bowel, thus absolutely discrediting any test based upon a specific relation between it and the gastric juice. Indeed, none of the methods of measuring the functional power of the gastro-intestinal tract which depend upon this principle have stood the test of time and practical experience.

In the case of achylia that I report (Case III) nuclei were quite constantly present, and yet there was nothing in the history, physical examination, character of the stools, or course of the disease for the year during which the patient has been under observation to suggest pancreatic disease The decidedly positive nucleus test in this case suggests that the digestion of the nuclei of muscle is not simply a matter of the presence or absence of the pancreas, as Schmidt assumes. The stools in this case showed a general lowering of the digestive force, not only for nuclei and muscle, but also for connective tissue and starch; and it seemed possible that the

nuclei survived because the pancreatic secretion was entirely absent. In the same way muscle fibers were not digested in the case I report in my other paper before this meeting, not because the pancreas was absent but because the power of digesting muscle in the intestine was temporarily inhibited, whether the fault lay in the absence of trypsinogen or its activating ferment enterokinase.

Finally, I wish to express my obligation and gratitude to Professor John H. Musser for the privilege of reporting Case I, II, III, VI, VII, and VIII, from his services in the Hospital of the University of Pennsylvania and Presbyterian Hospital in Philadelphia.

Conclusion. The nucleus test is probably a rough indication of the presence or absence of pancreatic secretion, but the case of achylia to which I refer and the result of our preliminary experiments upon dogs suggest that the relation between the nuclei of muscle and pancreatic digestion may not be specific, and that persistence of nuclei may be the result of general lowering of all digestive power quite as much as a sign of insufficiency of the pancreas alone.

EXPERIMENTS UPON DOGS.

This work was done by Dr. George P. Müller and myself in the Laboratory of Surgical Pathology of the University of Pennsylvania and is in a measure a preliminary report. Dr. Müller will publish the results of a further series of observations in the future.

Normal Dogs. 1. Meat-balls passed in twenty-three hours, fragmented, no nuclei.

2. Meat-balls passed in thirty-six hours, fragmented, no nuclei.

3. Meat-balls passed in thirty-six hours, fragmented, no nuclei.

4. Meat-balls passed in twenty-three hours, fragmented, no nuclei.

5. Meat-balls passed in twenty-three hours, fragmented, no nuclei.

Dogs Operated Upon. 1. Half of pancreas tied off. Meat-balls passed in thirty-six hours, fragmented, no nuclei.

2. Two-thirds of pancreas tied off. Meat-balls passed in twenty-four to forty hours, fragmented, no nuclei.

3. Whole pancreas tied off. Meat-balls passed in thirty-six to forty-five hours. Only one fragment large enough to examine. This contained nuclei.

4. Whole pancreas tied off. A series of meat-balls passed within eighteen to twenty-four hours, fragmented and showed no nuclei.

CLINICAL OBSERVATIONS.

Case I.—Male, white, aged fifty-seven years, canal boatman. (Reported from the service of Professor John H. Musser, Hospital of the University of Pennsylvania.)

Summary. Cholelithiasis and pancreatitis. Nucleus test positive. The patient had had jaundice with loss of weight and strength extending over eight months. He had always been healthy previously. There had been no symptoms of cholelithiasis. He had had dull epigastric pain and indefinite symptoms of indigestion. No fever. Stools were very fatty and showed slight impairment of splitting and very poor absorption. Good meat and starch digestion. A palpable tumor in the region of the gall-blader which was somewhat masked by muscular rigidity. Seven observations of the nucleus test showed all the nuclei intact at every trial. The time of passage of the meat-balls was between eighteen and twenty hours in every case. There was no diarrhœa. Operation showed cholelithiasis with ball-valve obstruction at the upper end of the common duct. The common duct was patulous below the stone. The tumor was formed by the head of the pancreas, which was hard, firm, and evidently the seat of chronic inflammation. No evidence of carcinoma and no evidence of complete closure of the pancreatic duct. Six weeks after the operation patient had recovered almost entirely.

March 30, 1906. J. K., white, male, aged fifty-seven years, native of Ireland.

Social History. Ever since the patient was eleven years old he has worked around canal boats. His work has not been very hard, but it has been exposing. He has used alcohol freely and tobacco to excess. He has had a fair amount of food all his life. The patient has no recollection of ever having had any of the diseases of childhood, and does not remember of ever having been sick until he was thirty-six years old, when he had what he calls intermittent fever, but was not jaundiced, and had no abdominal pain with it. About nine years ago he was in bed with fever that he was told "almost became typhoid," and just after he was well he had a severe pain in the right hypochondrium. This pain lasted three hours, and he was not jaundiced. He had never had typhoid fever, rheumatism, scarlet fever or pneumonia. He had gonorrhœa once, and once he had a sore on his external genitalia.

History of Present Illness. In August, 1905, the present illness began. The patient noticed that he was weak, and about the middle of August he was told he was yellow; after that he noticed it himself. He had some epigastric pain but no vomiting. He also noticed that his stools were light and his urine dark, and that the jaundice became deeper. His chief subjective symptoms were fulness and dull epigastric pain after eating, itching, and weakness. On September 1st he went to bed and was there five weeks, and when he got up he had lost considerable weight. From the middle of December to the middle of February, 1906, his weight came up a little and he felt stronger, but he always had a little jaundice. The middle of February he began to have a dull

burning in his stomach, which was followed by a renewed loss of weight and an increase in the jaundice. He went to the Presbyterian Hospital on March 8, 1906 (under the care of Professor Musser), complaining of loss of weight and strength, dull pain in his stomach, especially after eating, light stools, dark urine, deep jaundice, itching, and a vague mass in upper right abdominal quadrant. While at the Presbyterian Hospital his condition remained unchanged. The physical examination of his thorax was negative. Abdomen was soft and relaxed. There was some fulness noted along the upper third of the right rectus muscle. No visible peristalsis. There was some rigidity of the right upper abdominal quadrant, and a mass, which was hard, but of vague outline, was easily palpable. This mass began at the free costal margin, between the eighth and ninth ribs, and extended down to within a half-inch of the umbilicus; on the left it reached the midline; on the right it reached the midclavicular line. This mass was somewhat tender. Liver dulness reached from the sixth rib to the free costal margin; the organ was not palpable.

Urine. A faint cloud of albumin; no sugar. Microscopically, there were numerous calcium oxalate crystals, and numerous granular casts. Dr. Fife reported that the urine contained a great deal of urobilin but no unaltered bile. Two freshly passed samples of urine did not show the pancreas reaction of Cammidge. At the time this test was tried the patient was upon the full house diet with three ounces of olive oil daily in addition. This constituted the most favorable condition for eliciting the test according to Lovat (*British Medical Journal*, February, 1906).

Stomach. Normal in position and size. Motor power apparently normal. An Ewald breakfast removed in forty-five minutes (two observations) showed an acidity of the higher grade (Ta. 68, free HCl 32, and Ta. 95, free HCl 25).

Blood. Hemoglobin, 70; red blood corpuscles, 4,206,000; white blood corpuscles, 7360. Differential count normal.

Stool. Examination of stool when on ordinary mixed diet: stools are yellowish-white and fatty; upon exposure to air they turn brown. Bichloride test for bile shows little present. Reaction faintly acid. There is considerable neutral fat. There is moderately good starch digestion.

The patient was put on the Schmidt diet with which his stools showed some constipation, good digestion, but insufficient absorption of fat. No occult blood was found in five or six examinations; the reaction was sometimes acid, and sometimes alkaline; some bile was present. The stool was like butter and could not be washed off the glass with water. Patient was then given three ounces of olive oil a day, in addition to the normal diet. After this he showed a little neutral fat and a great excess of soap and fatty acid crystals, that is to say, the fat-splitting function was well preserved, but absorption was imperfect.

April 11, 1906. Operation to-day by Dr. Martin. There were found several small white spots upon the surface of the liver about 10 mm. in diameter, which looked like thickening of the capsule of the liver; the liver itself was not enlarged. The gall-bladder was small and shrunken, and was entirely filled by a large round stone. The cystic duct was obliterated. The hepatic duct was much dilated, and in the common duct one inch below its beginning there was a large round stone, about the size of that in the gall-bladder, namely, 3 cm. in its long diameter and 2 cm. in its short diameter. About an inch farther down there was a still larger stone which appeared to form a ball-valve obstruction in the common duct; the duct below the obstruction was slightly dilated, as if there had been another stone in it at some time which had been passed. The duct below the stone was patulous at the time of operation; a probe was passed through it into the duodenum without difficulty. The head of the pancreas was swollen to twice its natural size, was hard and not nodular; the glands were not swollen in its neighborhood.

Dr. Martin's clinical diagnosis was *subacute pancreatitis*, and not carcinoma. The head of the pancreas formed the tumor that was felt before operation in the region of the gall-bladder.

Nucleus test made before operation. 1. Meat-ball eighteen hours, nuclei intact, test positive.

2. Meat-balls eighteen hours, nuclei intact, test positive.
3. Meat-balls twenty hours, nuclei intact, test positive.
4. Meat-balls twenty hours, nuclei intact, test positive.
5. Meat-balls eighteen hours, nuclei intact, test positive.
6. Meat-balls eighteen hours, nuclei intact, test positive.

Case II.—Male, aged forty-eight years, white, printer. (Reported from the Service of Professor John H. Musser, Hospital of the University of Pennsylvania.) Carcinoma of the head and body of the pancreas. The patient had had jaundice with chills and fever for nine weeks. No pain or vomiting. Poor digestion. Great loss of flesh and strength. Stools fatty and good splitting. First operation showed hardening and enlargement of the head of the pancreas but no nodules. No gallstones. Biliary fistula established. Much improved in general condition and gain of sixteen pounds in weight. The second operation was undertaken to close the biliary fistula. At this time the head and body of the pancreas were found to be hard and nodular, probably carcinomatous. Biliary fistula retained. The stools were white, very bulky, constipated and very fatty, with poor, but not absent, splitting. The stool consisted almost entirely of soaps and fatty acid crystals with some neutral fat. Nine observations of the nucleus test showed absence of nuclei except in one meat-ball. The test was considered negative. The time of passage of the meat-balls was between twenty and twenty-four hours in every case. This excluded bacterial action as a reason for the disappearance of the nuclei. Third

operation was undertaken to connect the gall-bladder with the small intestine. At this time the mass in the head of the pancreas was harder and more nodular. Common bile duct was completely obstructed. The stool was very fat with poor splitting and excess of fats and soaps, otherwise good digestion.

G. W. P., aged forty-eight years, white; occupation, printer. Patient had used tobacco in moderation and alcohol only occasionally. He had never been intemperate in his eating. Denies venereal disease. The patient had never had a serious illness until the commencement of the present attack. Nine weeks before he had a chill which lasted for an hour and was followed by fever. Two days later he had another attack of a similar character. There was no pain, tenderness or jaundice. For two weeks after this he felt very well and continued at work, but at the end of this time he noticed that his eyes and skin were becoming yellow. This jaundice persisted seven weeks until admission. There was no pain and no vomiting. Stool was clay colored and urine was dark. He was very constipated. He had lost forty-two pounds. He had become much weaker since the commencement of the attack. He had no appetite.

Physical examination of the thorax was quite negative. Patient was jaundiced. The liver dulness reached from the sixth rib to four fingers' breadth below the margin of the ribs in the right nipple line. It extended to within an inch of the umbilicus in the median line, and extended to the left as far as left nipple line. The organ was quite distinctly palpable posteriorly. In the region of the gall-bladder, which was of course displaced downward, there was a distinct visible and palpable fulness, and around and about this fulness there was a distinct notch in the liver, apparently the notch for the gall-bladder, making it seem very probable that the mass was the distended gall-bladder. Gallstone crepitus could not be elicited.

Urine. Very dark in color; specific gravity, 1016; heavy cloud of albumin, no sugar, some bile. Microscopically, hyaline and granular casts and some leukocytes, all stained yellow.

Blood. Hemoglobin, 47 per cent.; red blood corpuscles, 3,420,000; white blood corpuscles, 28,000. Differential count showed an increase in polymorphonuclear cells only.

Stomach. Normal in position and size; motor power normal, Ewald test meal extracted in one hour shows a subacidity (Ta. 14, free HCl 12). No lactic acid.

Stools. Clay colored; microscopically; an excess of soaps and fatty acid crystals.

October 20, 1905. Operation by Dr. Martin. The gall-bladder found to be considerably distended. Exploration showed something that felt like a stone in common duct, but it slipped away and could not be found again. The head of the pancreas was possibly slightly larger than normal, but nothing positive was found, and it did not seem enough to afford obstruction to the common duct; no tumors were discovered. At this time it was deemed advisable to do no more than drain the gall-bladder, so the abdominal wound was closed in the usual manner, the gall-bladder brought up out of the wound, the edges sutured to the skin edges and a drainage tube inserted.

December 13th. Patient was discharged to-day improved. He has gained twelve pounds in weight. Discharge of bile still present.

March 25, 1906. Patient has been re-admitted in order to have his biliary fistula closed. Since leaving the hospital he has gained four more pounds in weight and greatly in strength. The biliary fistula still persists and discharges quite profusely. At times his stools have been clay colored, and at others brown. Skin conjunctivæ are slightly jaundiced. Hemoglobin, 49.

28th. Second operation. The liver was adherent to abdominal parietes. On exploration head of pancreas was hard and enlarged (evidently carcinomatous). The gall-bladder was opened, and the common duct was dilated. Careful efforts were made to find a stone but none was present. A No. 12 English catheter was passed through the obstruction of the common duct, which obstruction was produced by a new-growth continuous with pancreas. A tube was inserted into the opening of the common duct, and held there with catgut sutures; the gall-bladder was drained with tube.

Dr. Martin made a positive diagnosis of carcinoma of the head of the pancreas, but it will be noticed that the bile duct was not totally occluded and there was no evidence that the pancreatic secretion was entirely cut off.

The patient had gained sixteen pounds in the intervals between the first and second operation and has held his weight very well since the last operation. He was not cachectic. His hemoglobin was higher and he was in surprisingly good condition. He had no symptoms referable to the gastrointestinal tract. His appetite was good and he enjoyed his food. Although a positive clinical diagnosis of pancreatic carcinoma was made, the condition of the patient was so good that we may assume either that the malignant disease was as yet not very widespread, or that the diagnosis of malignant disease might have been wrong.

Stools. The examination of his stool while on the ordinary light diet of the hospital was as follows: Very constipated and copious, white or grayish-white; very offensive; alkaline; no bile; good muscle, connective tissue and starch digestion. As seen when microscopic specimens were made, some neutral fat, excess of soaps and fatty acid crystals. Some difficulty in splitting and very poor absorption. No meat fiber.

Meat-balls. 1. Seventeen hours, nuclei almost intact.

2. Meat-balls. 1. Seventeen hours, nuclei almost intact.

2. Twenty-seven hours, no nuclei.

3. Twenty-seven hours, no nuclei.
4. Nineteen hours, no nuclei.
5. Nineteen hours, no nuclei.

May 1, 1906. Patient was again operated upon. The common bile duct was found to be totally occluded. The head of the pancreas was hard and larger than at the second operation and was more evidently carcinomatous. A fistula was made between the gall-bladder and the small intestine. As soon as the patient recovered from the effect of the operation his stools were again examined and found to be in the same condition as between the first and second operation, namely, a very fat stool with poor splitting, poor absorption, but a very good starch and meat digestion.

A nucleus test was tried with the following result:

6. Twenty-seven hours, no nuclei, test negative.
7. Twenty-four hours, no nuclei, test negative.
8. Twenty-four hours, no nuclei, test negative.
9. Twenty-four hours, no nuclei, test negative.

Case III.—(Reported from the Service of Professor John H. Musser, Presbyterian Hospital in Philadelphia.) Achylia completa, with hyperesthesia of gastric mucous membrane, probably neurosis of stomach. History of general nervous irritability and irregular and atypical gastric symptoms.

Stomach Contents. Absence of all secretion, acid, and ferments.

No blood; no retention, no lactic acid.

Stools. Connective tissue of beef-steak visible to naked eye but not in large amounts; stool lumpy and watery; poor starch digestion; no excess of soap; no neutral fat; no mucus; no blood; no excess of muscle.

Physical Examination. Thorax and abdomen negative; blood; secondary anemia of moderate degree.

Subsequent Course. Improves when on rest cure but relapses when he goes to work. No signs of cancer or pancreatic disease have developed.

Nucleus Test. 1. Meat-ball, eighteen hours, nuclei intact.
2. Meat-ball, eighteen hours, many nuclei.
3. Meat-ball, seventeen hours, nuclei intact.
4. Meat-ball seventeen hours, nuclei intact.

Case IV.—Cholelithiasis and enlargement and hardening of head of pancreas as shown by operation in November, 1905.

March, 1906, stool not fatty, no azotorrhœa.

1. Meat-ball, nineteen hours in passage, few nuclei, test negative.
2. Meat-balls, nineteen hours in passage, few nuclei, test negative.

Case V.—Achylia completa, arteriosclerosis; syphilis; alcoholism.

1. Meat-ball, eighteen hours, absent nuclei.
2. Meat-ball, eighteen hours, absent nuclei.

Case VI.—Carcinoma of pleura.

1. Meat-ball, eighteen hours, absent nuclei.

Case VII.—Male, aged forty years; hepatic cirrhosis in advanced stages; ascites; mitral regurgitation; edema of legs; jaundice; stools showed an excess of soaps and fatty acids and some neutral fat; no blood; otherwise good digestion; no excess of muscle fibers.

Nucleus Test. 1. Meat-ball, twenty hours, no nuclei.
2. Meat-ball, twenty hours, no nuclei.
3. Meat-ball, twenty-four hours, no nuclei.

Case VIII.—Woman, aged forty-five years; cholelithiasis; operation by Dr. J. B. Deaver, who found undoubted evidence of pancreatic disease (enlargement and hardening of organ); diabetes developed one month after operation and had continued for two years when nucleus test was made; stools showed good digestion and absorption of fats and muscle.

Nucleus Test. 1. Meat-ball, twenty hours, no nuclei.

Case IX.—Normal. (Dr. D.)

1. Meat-ball eighteen hours, no nuclei; test negative.
2. Meat-ball, eighteen hours, few nuclei; test negative.

Case X.—Normal. (Dr. S.)

1. Meat-ball, ten hours, nuclei intact.
2. Meat-ball, ten hours, nuclei intact. This observation is of no value since too short a time was given for the digestion of the nuclei.
3. Meat-ball, twenty-two hours, few nuclei; test negative.
4. Meat-ball, twenty-two hours, few nuclei; test negative.
5. Meat-ball, twenty-two hours, absent nuclei; test negative.

Case XI.—Normal. (Dr. G.)

1. Meat-ball, twenty hours, nuclei intact.
2. Meat-ball, twelve hours, nuclei intact. This observation is of no value since too short a time was given for the digestion of the nuclei.
3. Meat-ball, twenty-four hours, no nuclei.
4. Meat-ball, twenty-four hours, no nuclei.

Case XII.—Normal. (Dr. B.)

1. Meat-ball, fourteen hours, no nuclei.
2. Meat-ball, fourteen hours, no nuclei.

NITROGEN EVOLVED FROM ALKALINE SODIUM HYPOBROMITE SOLUTIONS.

By John Marshall, M.D.,
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and
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Assistant Demonstrator of Chemistry, University of Pennsylvania.

(From the Robert Hare Laboratory of Chemistry, Department of Medicine, University of Pennsylvania.)

In the determination of urea by the Knop-Hüfner alkaline hypobromite method, oxygen is evolved simultaneously with the nitrogen derived from the urea in as short a space of time as two and a half minutes devoted to the performance of the method.[1] The longer the time devoted to the performance of the method the greater is the volume of oxygen yielded. This oxygen is derived from the decomposition of some of the hypobromite itself and also probably from atmospheric oxygen dissolved in the aqueous solution of the hypobromite. On permitting a volume of about 125 c.c. of an aqueous solution of sodium hypobromite containing free alkali prepared of the strength designated by Knop (*i. e.*, by dissolving 100 grams of sodium hypobromite in 250 c.c. of distilled water, allowing the solution to cool and then gradually adding 25 c.c. of bromine at the same time, keeping the liquid cool by holding the glass cylinder in which it is contained under a stream of cold water), to stand a number of hours, a measurable volume of oxygen may be obtained. This constitutes one of the fallacies of the Knop-Hüfner methods for the quantitative determination of urea.

On allowing an aqueous alkaline solution of sodium hypobromite to stand several hours under ordinary conditions of temperature, and collecting the evolved gas, and treating the latter with an alkaline pyrogallol solution we noticed that a small volume of gas refused to be absorbed by the alkaline pyrogallol solution. This residual gas was transferred under mercury to a Bunsen endiometer containing mercury. A cubic centimeter of distilled water and several volumes of electrolytically obtained oxygen were introduced and the mixture of gases was sparked, whereupon a gradual diminution of volume occurred and, after the expiration of an hour, the water was removed from the endiometer and tested with litmus paper. The liquid was found to be acid in reaction, and to respond to the ferrous sulphate ring-test for nitric acid, thus demonstrating that the residual gas which refused to be absorbed by the alkaline pyrogallol solution consisted of nitrogen.

The origin of this nitrogen seemed to us to be worthy of investigation and the following experiments detail the results we obtained:

Our first quest was for the presence of ammonium compounds as a source of nitrogen in the substance employed in the preparation of the hypobromite solution. For this purpose 180 grams of sodium hydroxide, in sticks, such as we proposed using in the experiments, were dissolved in 450 c.c. of ammonia-free distilled water and placed in a tubulated glass flask and distilled. The distillate was collected in 50 c.c. of $\frac{n}{10}$ hydrochloric acid until the total volume amounted to 250 c.c., and 50 c.c. of it titrated with $\frac{n}{10}$ sodium hydroxide required exactly 10 c.c., thus demonstrating that the distillate contained no ammonia. Portions of the distillate as they were collected during the period of distillation were tested with litmus paper without giving evidence of alkalinity. 100 c.c. of the distillate were treated with platinic chloride and evaporated to dryness on a water-bath and the residue was treated with alcohol with the result that the entire mass dissolved, showing that no ammonium platinic chloride had been formed.

The next substance examined for the presence of ammonia was the bromine, such as was to be employed in the experiments. To accomplish this, 310 c.c. of bromine were placed in a glass tubulated distilling flask stoppered with a caoutchouc stopper, which had been previously coated with a thin pellicle of vaseline, and the flask was then connected with a Liebig's condenser in such a manner as to prevent the bromine vapor coming in contact with the vaseline-coated caoutchouc connection. Distillation was continued until the residual bromine in the distilling flask measured about 15 c.c. This residual bromine, together with several portions of ammonia-free water used as wash-water, was poured into a glass cylinder provided with a vaseline-coated perforated caoutchouc stopper through the perforations of which two glass tubes were introduced, one tube passing to the bottom of the cylinder and the other about 2 cm. below the stopper. Air, which had been previously passed through a Woulff bottle containing strong sulphuric acid was drawn through the bromine containing liquid at ordinary temperature until all the free bromine had been removed, as evidenced by the complete decolorization of the

[1] Ryan and Marshall. Univ. of Penna. Med. Bulletin, February, 1905.

liquid. There still remained in the distilling flask a white residue, insoluble in water. This was treated in turn with alcohol and ethyl ether in which solvents the entire residue dissolved. These solutions were evaporated to dryness at a low temperature and the dry residue was scraped from the dish and added to the decolorized liquid above mentioned. This liquid containing the added white, insoluble material was placed in a tubulated distilling flask, rendered alkaline with solid potassium hydroxide (purified by alcohol), and distilled into 200 c.c. of ammonia-free water contained in an Erlenmeyer flask attached to the condenser and provided with an additional flask containing distilled water to prevent access of ammonia from the atmosphere. Distillation was continued until about 40 c.c. of distillate had passed into the 200 c.c. of water. This was then diluted to 250 c.c. by the addition of ammonia-free water. 100 c.c. of this solution placed in a Nessler's tube and tested with Nessler's solution yielded a color corresponding in intensity with that produced by 100 c.c. of an ammonium chloride solution containing 0.00034 gram of NH_3, therefore, the 250 c.c. of diluted distillate must have contained 0.00085 grams NH_3. Distillation was continued and the distillate was collected under the precautions described above in an Erlenmeyer flask containing 100 c.c. of ammonia-free water until the total volume in the flask amounted to 150 c.c. A small part of the last portion of distillate was tested with Nessler's solution without result. The 150 c.c. were then diluted with ammonia-free water to a volume of 250 c.c. 100 c.c. of this solution placed in a Nessler's tube and treated with Nessler's solution yielded a color corresponding to 0.00004 grams of NH_3, therefore the 250 c.c. must have contained 0.0001 gram of NH_3. The summation of these two quantities 0.00085 + 0.0001 equals 0.00095 grams NH_3, equivalent to 0.000782 gram of nitrogen corresponding to 0.622 c.c. of nitrogen; consequently 310 c.c. of bromine contained ammonium salts equivalent to 0.622 c.c. of nitrogen.

GAS EVOLVED FROM AN ALKALINE SOLUTION OF SODIUM HYPOBROMITE PREPARED ACCORDING TO THE FORMULA OF KNOP ON STANDING 212 HOURS.

The alkaline sodium hypobromite solution, prepared as described in the forepart of this article, was placed in a Bunsen gasometer[1] of 600 c.c. capacity provided with a glass stopcock to which was attached a double goose-neck glass tube, of very small lumen. The lower goose-neck dipped under water and over its end was placed a small glass tube filled with boiled distilled water to collect the evolved gas. The glass tube attached to the gasometer was filled, as well as the entire apparatus, with the hypobromite solution. The tube was attached to the gasometer by means of a caoutchouc tube which had been coated with a slight pellicle of vaseline and was in intimate contact with the glass neck of the stop-cock of the gasometer so that only the slightest surface of the caoutchouc (coated with vaseline) was in contact with the solution.

After the expiration of 212 hours, the volume of gas collected in the small tube was transferred over water to an endiometer containing water and allowed to stand several hours with the opening of the endiometer just below the surface of the water, in a large beaker to permit the sodium hypobromite coming from the small tube in transferring the gas, in the endiometer to diffuse into the large volume of water in the beaker. The volume of gas corrected for 0° C. and 760 mm. pressure and tension of aqueous vapor, measured 17.06 c.c. This gas was then transferred over mercury into an endiometer containing mercury and while in the endiometer, was treated with an alkaline solution of pyrogallol. After absorption of the oxygen contained in the gas by the alkaline pyrogallol the endiometer was suspended over water to permit the pyrogallol solution to diffuse into the water in the beaker. The residual gas measured and corrected for 0° C. 760 mm. pressure, and tension of aqueous vapor amounted to 3.34 c.c. The gas was then transferred over mercury into a Bunsen endiometer containing mercury and into which about 5 c.c. of water were introduced. To this volume of 3.34 c.c. of gas, supposed to be nitrogen, 7.5 c.c. of oxygen were added and the mixture was sparked until the space occupied by the residual gas was about 2 c.c. or the space containing the platinum electrodes. The water above the mercury in the endiometer was removed and found to be acid in reaction. The acid liquid was neutralized with chemically pure sodium carbonate and evaporated to dryness on a water-bath. The residue thus obtained was dissolved in about 5 c.c. of distilled water, was rendered distinctly acid with sulphuric acid, cooled and a small crystal of ferrous sulphate was introduced, whereupon a decided brownish coloration surrounding the crystal was produced indicating the presence of nitric acid and that the residual gas which refused to be absorbed by the alkaline pyrogallol solution consisted of nitrogen.

As it had been previously determined that the source of this nitrogen could not be ammonium compounds possibly contained in the sodium hydroxide used in preparing the sodium hypobromite solution, and that the bromine, used for the same purpose, although containing ammonium compounds contained the latter in quantity inadequate to account for the volume of nitrogen yielded by the hypobromite solution we are restricted to the atmospheric nitrogen dissolved in the hypobromite solution as the source of the nitrogen. During the slow evolution of oxygen from the auto-

[1] Bunsen, Gasometrische Methoden, 1877, p. 23.

decomposition of the sodium hypobromite, nitrogen from the air which had been in solution in the liquid must have been gradually removed from the liquid by the larger quantity of escaping oxygen.

In this experiment a solution of 600 c.c. of the alkaline hypobromite solution was employed, and the volume of nitrogen collected was 3.34 c.c. at 0° C. and 760 mm. pressure. If by calculation this volume were converted into the volume the gas would occupy at 20° C. (760 mm. pressure) the result would be 3.58 c.c. 1 c.c. of water at 20° C. and 760 mm. pressure, will hold in solution 0.01704 c.c. of air[1] in which volume the proportion of nitrogen to oxygen is as 1.87 of nitrogen to 1 of oxygen,[2] therefore, 600 c.c. of water would hold in solution 6.66 c.c. of nitrogen. The volume of nitrogen yielded by the ammonium salts contained in 310 c.c. of bromine such as was employed in these experiments, as before stated, amounted to 0.622 c.c. As in the preparation of the 600 c.c. of hypobromite solution employed, 60 c.c. of bromine were used, the latter quantity of bromine would have yielded 0.12 c.c. of nitrogen, therefore, the difference between this volume and 3.58 c.c. or 3.46 c.c. must be attributed to the nitrogen which has been contained as dissolved atmospheric nitrogen in the solution. The experiment with the 600 c.c. of hypobromite solution was conducted at a temperature of about 20° C. and if the liquid had been pure water instead of hypobromite solution we might expect to obtain under the same conditions not more than 6.66 c.c. of nitrogen. The coefficient of absorption of nitrogen by an alkaline hypobromite solution of the concentration employed in the experiment is unknown, but it is probable that the solubility of nitrogen in such a solution is considerably less than in pure water.

After having determined the identity of the residual gas which refused to be absorbed by the alkaline pyrogallol solution, a series of experiments was conducted to ascertain the relative volumes of nitrogen and oxygen evolved by alkaline sodium hypobromite solution on standing various periods of time. The apparatus employed in these experiments was the Hüfner[1] apparatus designed for the determination of urea in urine. The evolved gas was transferred to an endiometer over mercury and the oxygen was absorbed by means of an alkaline solution of pyrogallol. The following table gives a summation of the results:

Relative Volumes of Nitrogen and Oxygen Evolved from Alkaline Sodium Hypobromite Solutions on Standing Various Periods of Time.

Hours standing.	Hypobromite vol. c.c.	Total gas evolved at 0° and 760 mm. c.c	Nitrogen vol. at 0° and 760 mm. c.c.	Oxygen vol. at 0° and 760 mm. c.c.
43	117	1.48	0.7	0.78
73	121	4.92	0.3	4.62
72	117	9.51	0.5	9.01
72	121	9.59	0.67	8.92
72	121	7.07	0.26	6.81
72	117	9.27	0.88	8.39
72	112	5.9	0.26	5.64
137	117	22.5	2.03	20.47
137	121	26.1	1.85	24.25

[1] Chem. Kalendar, 1903, p. 256.

[2] Remsen, Inorganic Chemistry, 1898, p. 251.

[1] Hüfner, Journ. f. prakt. Chem., Neue F., Bd. iii, p. 1.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James E. Rogers Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

AN ADDRESS ON SANITATION IN THE JAPANESE NAVY AND ARMY.

By Baron K. Takaki,

Director of the Medical Bureau and Surgeon-General of the Imperial Japanese Navy.

[Note.—The address on "Naval and Military Sanitation," by Baron Takaki, was delivered before the faculty and students of the Medical Department of the University of Pennsylvania, 1906.

The address was arranged for publication by Dr. D. H. Bergey and, as it appears here, has had eliminated from it some of the tabulated material showing the numerical strength and official classification of the members of the Japanese Navy and Army, as well as a number of tables giving details with regard to the former and the present diet used in the Navy. These tables were omitted because it was felt that it would not detract from the general usefulness of the address as a whole and would still permit of the presentation of the details of interest to the reader.

The Japanese term for beriberi is kakke, and throughout the address the Japanese term has been retained.]

NAVAL SANITATION.

The subject of my address here is the same as in the Cartwright Lecture, the reason being that on this subject I may claim to have some practical experience and knowledge on account of my long service in the Navy.

Here, I have two tables showing various details regarding the health of the Navy from 1878-1902 and I am now going to explain all the details:

Table I.—*Number of Deaths for each Year from* 1878 *to* 1902.

Year.	Death from All causes.	Death from Diseases alone.	Ratio per 1000 of force. All causes.	Ratio per 1000 of force. Diseases alone.
1878	56	51	12.37	11.26
1879	119	118	23.42	23.22
1880	63	58	12.71	11.70
1881	81	80	17.45	17.24
1882	103	100	21.59	20.97
1883	85	78	15.89	14.59
1884	45	42	7.98	7.45
1885	49	43	7.08	6.22
1886	63	58	7.43	6.25
1887	55	37	6 04	4.06
1888	65	42	7.08	4.57
1889	52	45	5.81	5.03
1890	78	53	8.56	5.82
1891	60	51	5.87	4.99
1892	135	61	7.59	6.26
1893	56	49	6.01	5.26
1894	165	40	15.00	3.64
1895	193	126	14.84	9.69
1896	139	87	10.66	6 67
1897	103	77	6.88	5.15
1898	129	92	7.00	4.99
1899	118	95	6.04	4.86
1900	107	74	4.59	3.18
1901	136	97	5.14	3.66
1902	154	126	5.06	4.14

Table II.—*Cases of Kakke and Ratio of Deaths per* 1000 *of Strength in the Navy for each Year from* 1878 *to* 1902.

Year.	Cases.	Ratio of cases per 1000 of force.	Dead.	Ratio of deaths per 1000 of force.	Invalided.	Ratio of invalided per 1000 of force.
1878	1485	327.96	32	21.55	Uncertain.	Uncertain.
1879	1978	389.29	57	28.82	8	4.04
1880	1725	348 06	27	15.65	9	5.21
1881	1163	350.59	30	25.80	16	13.76
1882	1929	404.49	51	26.44	17	8.81
1883	1236	231·20	49	39.64	4	3.24
1884	718	127.35	8	11.14	1	1.39
1885	41	5.93	...	...	1	24.39
1886	3	0.35				
1887						
1888						
1889	3	0.34	1	333.33		
1890	4	0.44				
1891	1	0.10				
1892	3	0.31				
1893	1	0.11				
1894	29	2.64	2	68.97		
1895	17	1.31	1	58.83		
1896	11	0.84				
1897	22	1.47	2	90.91		
1898	16	0.87	1	62.50		
1899	6	0.31				
1900	10	0.43				
1901	14	0.53				
1902	32	1.05				

The average number of general diseases during 1878, 1879, 1880 was 4327 per thousand, that is, one sailor suffered 4.32 times every year. The death rate averaged 16.34 per thousand and the invaliding rate 8.75.

The number of kakke patients (Table II) was 349.33 per thousand. Those who died from it averaged 7.96, and those invalided, 2.45 per thousand. Therefore, the number of sailors lost through death and made invalids owing to general diseases was 24.09 per thousand and those lost through death and invaliding from kakke, 10.43 per thousand. If we now subtract 10.43 from 24.09 only 13.66 remains. Hence, it was clear that if kakke could be wholly exterminated, the number of losses from illness would decrease to 13.66.

From 1881 to 1883 the number of cases of illness slightly decreased. In 1884 the general aspect of the health of the navy suddenly changed for the better and the number of general diseases as well as cases of kakke markedly decreased. The number of general diseases was 1776.27 per thousand, that is, one person became ill 1.77 times a year. Deaths per thousand decreased to 7.98, and invalids to 7.80. The number of kakke cases averaged 127.35 per thousand. Deaths from it decreased to 1.42. Therefore, the average of deaths and invalids from general diseases decreased to 15.78 and that of kakke to 1.60 per thousand. Similarly,

in 1885, the number of general diseases decreased to 992.48 per thousand, and deaths to 7.08 per thousand. Kakke decreased to 5.93 per thousand without death. So the number of deaths and invalids decreased to 12.14. In 1886 general diseases per thousand averaged 577.46, deaths 7.43, and kakke 0.35 without death or invaliding. In 1887 general diseases were 434.22, deaths, 6.04, and invalids, 6.15 per thousand. In 1888, general diseases averaged 400.59, deaths, 7.08, and invalids, 9.15 per thousand.

In short, the number of losses through deaths and invalids in 1884 was 15.78; in 1885, 12.14; in 1886, 12.57; in 1887, 12.19; in 1888, 16.33 per thousand. If we now compare these five years to three years from 1878 to 1880 we find a marked decrease of general diseases and disappearance of kakke with corresponding decrease in the loss of sailors year by year. These good results must depend upon certain causes and in order to explain them I will first of all try to describe various important facts since the establishment of the Naval Medical Bureau in 1872.

The Establishment of the Naval Medical Bureau.

The Naval Medical Bureau of the Japanese Empire was established for the first time in 1872. At that time there was no one who had a thorough idea of naval hygiene, because up to that time there was no special sanitary work carried out by medical officers in our navy, and other officers thought that the necessity of medical men in the navy was simply for treating diseases and wounded. Even the medical officers thought in the same way. They never had the slightest idea of doing anything in preventing the disease or in general hygiene. Accordingly, the only medical record. left from 1872 to 1877 was limited to the description of results of treatment, name of diseases, and names of patients taken into hospitals. Between 1878 and 1883 the record gradually began to include facts about hospital and non-hospital patients and some hygienic affairs. Finally, from 1884 the records became more and more complete, giving various tables illustrating hygienic conditions by the issue of the instructions relating to the duties of the medical officers.

The Education of Naval Officers.

At the time of the establishment of the Medical Bureau, in 1872, Dr. Wheeler, attached to the British Legation, was invited by the Naval Hospital to give lectures, both theoretical and practical. In 1872 Dr. William Anderson was specially invited from England to teach medical officers and students. In 1877, sixteen men were qualified and passed out of the school. These were the first graduates. Chief among them were the present Surgeons-General Yamamoto, Totsuka, Suzuki, and Kimura. The first three were educated, like myself, in St. Thomas' Hospital for the higher course of study. (Surgeon-General Yamamoto served during the recent war with Russia as the Chief-Surgeon of Yokosuka Naval Station, Surgeon-General Totsuka as the Chief-Surgeon of Sasebo Naval Station, where the majority of the wounded from the naval fights were treated, and Surgeon-General Sazuki as the Chief Medical Officer of Togo's fleets.) However, later on during my absence in England, the levying of medical students was stopped and Dr. Anderson was discharged. It was then found that as the newly adopted medical officers could not understand a foreign language, they could neither learn anything about naval and military hygiene in foreign lands nor could they follow the progress of medical science in general. Besides, they could not talk and associate with foreign medical officers, and on occasions when they went to foreign ports or lands they could not find out the sanitary conditions, especially those relative to the endemic and epidemic diseases, of those ports.

Again this ignorance of foreign languages led to inconveniences in buying articles of food, drinking water, etc., and thus there was always fear of the invasion of infectious diseases through this channel. Moreover, the foreign language used by the Imperial University in teaching medicine was German, and I thought that the language most useful and important to our naval medical officers would be English. Finally, unless those who serve in the navy were able to keep up the general spirit characteristic of sailors, they could not work hand in hand with the fighting or deck officers and they would find many inconveniences in conducting sanitary affairs. Accordingly, I insisted upon re-establishing the naval medical school and enlisted some students in 1881. Besides the full medical course, the English language was taught as an extra subject, and by 1894 eighty students in all passed out as officers. But after that year (in 1893 I retired from active service, was placed in the reserve list, and became a member of the House of Peers) fresh students were not again enlisted and new medical officers were obtained from among those who studied in the Imperial University and specially licensed medical schools.

Medical officers were also sent abroad to pursue further study in medical science. In 1872, Drs. S. Ono and K. Yoshida; in 1874, Dr. T. Ishigami; in 1875, Dr. K. Takaki; and in 1878, Dr. A. Saneyoshi were sent to England.

Since then a number of medical officers were sent to Europe, chiefly to England and Germany.

I entered the navy in 1872 and began to treat sick and wounded. What at once attracted my notice was the large number of kakke patients and the numerous deaths resulting from it. And as this disease truly played havoc with the health of our navy and killed many, so as to greatly reduce

our fighting strength, I turned my attention toward finding its cause and treatment.

By doing so, I meant to prevent the outbreak of this disease and provide against unforeseen danger through ill-health in time of crisis in our Empire. In pursuing this purpose, I met with many difficulties and passed through years of hard work.

The first time I heard of the fearful nature of kakke was forty-four years ago. At that time guards were despatched by several Daimios to Kyoto to act as protectors of the Imperial Palace, and my father being one of them stayed there for over a year. On his return, he told me of the disease called kakke, which killed many of these men. They attributed the cause to food and called a provision box the "kakke box."

Later, in 1868, that is in the year of the Meiji revolution, I served for eight months in the army of Prince Shimadzu, but did not see any kakke. As I said before, I entered the navy in 1872, and began to treat kakke patients for the first time. Up to May, 1875, I had seen several hundred kakke cases at the Naval Hospital. In the summer several acute cases appeared daily. Often five or six cases had to be treated at the same time and attending officers had to work very hard both day and night. At that time the kakke patients constituted three-fourths of the whole number of patients. Various forms of treatment were adopted:

Purgatives; digitalis for œdema, palpitation, etc.

Strychnine, iron, etc, for numbness and paralysis.

Tincture of aconite for hypersensibility of muscles.

Purgatives; venesection for acute cases.

These forms of treatment were general and there was no definite opinion as regards the food.

Conditions being such, it became my fixed desire to discover the cause and treatment of kakke. But I thought that with my insufficient knowledge of medical science, I could not possibly discover them, and from then on, the desire to go abroad in order to fit me for attaining my object, never left my thoughts even for a moment. At last, in June, 1875, the desire was fulfilled and I started for England. I reached London in July and entered St. Thomas' Hospital Medical School in October. After staying there for over five years I returned to Japan in November, 1880, and was made the Director of the Tokyo Naval Hospital in December. Thus, I got an opportunity to treat kakke patients again. The general conditions on my return were exactly the same as before I went to England, and with subsequent increase of sailors more kakke cases appeared.

At times, when the disease was in full force, we found the hospital too small and often had to use neighboring temples. Moreover, acute cases were many and medical officers had a very busy and hard time. Such conditions used to strike my heart cold whenever I came to think of the future of our Empire, because if such a state of health went on without discovering the cause and treatment of kakke, our navy would be of no use in time of need.

As a first step toward the cause and cure of this disease, I began to note the localities and seasons and to examine sailors in ships, barracks, etc., and I obtained the following facts:

1. Kakke mostly occurred from the end of spring to summer, but it was not limited to the warm season, sometimes occurring during the severe cold of winter.

2. The occurrence of the disease varied in different ships, barracks, etc.

3. Even in the same ship, it appeared in some stations, not in the others, and was never certain.

4. It occurred from time to time without regard to the state of quarters or clothing.

5. I found out that although clothing, food, living, etc., were not quite the same in all stations, yet they were almost similar.

With these facts I could not easily discover the cause, and I went on with further investigations with the following results:

1. As regards the class of patients in general, I found that sailors, soldiers, policemen, students, shop-boys, etc., were those who suffered most.

The upper class rarely became affected.

2. The people living in the same place suffered unequally, that is, some suffered and others not.

3. Although it occurred mostly in large cities, like Tokyo, Osaka, and Kyoto, yet it sometimes appeared in other smaller towns as well.

Thus, with such results and without discovering the cause of kakke the time quickly passed to the year 1882. In February of the year 1882 I was appointed Vice-Director of the Naval Medical Bureau.

About that time it was found to be necessary to provide an extra medical officer besides the usual number on board the training ships for long cruises, on account of the abundance of kakke cases among the men during the voyage.

In 1882 there was a critical state of affairs with Corea and three warships were sent to Ninsen (Chemulpo) and Saibutsu Bay. They stayed there only forty days, but owing to shortness of hands caused by the prevalence of kakke among sailors, the officers felt quite unfit for battle and it was a very anxious time for those in positions of responsibility because those three ships would have been of no fighting value in the critical moment. For example in one of the ships 195 out of 330 were sick with kakke.

As a consequence, I handed to the chief of the Naval Medical Bureau, on June 24, 1882, a memorandum describing the facts.

Following this, in August, 1882, H. I. M. S. "Fuso," in spite

of anchoring off Shinagawa Bay had to send half of its crew ashore in turns for the treatment of kakke.

Continuing still farther, I examined the reports of the Tokyo and Yokohama Naval Hospitals for 1881, and found that three-fourths of the patients had suffered from kakke.

In 1883, I received permission from the minister of the navy to examine the hygienic conditions of ships, barracks, schools, etc., belonging to the navy. I found that although working hours, clothing, dwelling houses, etc., were similar everywhere, yet in food there was a great deal of difference. So, I now asked the head of each sectional department to send me in the reports describing the details of food taken three times daily for a week. From this I discovered the following facts:

1. Nitrogenous substances contained in the food were not sufficient to make up for the amount of nitrogenous substances discharged from the body.

2. On the contrary, the food contained too much carbohydrates. If we now examine a table recognized by scientists as showing the comparative amounts of nitrogen and carbon discharged daily by a fair-sized adult, we will see that carbon equals 310 grams and nitrogen equals 20 grams, *i. e.*, nitrogen is to carbon as 1 is to 15.5.

3. The food taken by our sailors showed nitrogen 1 to carbon 17.32.

4. The greater the difference in these proportions the more kakke occurred; and the lesser the difference, the less.

After obtaining these important facts I came to think that:

1. Kakke is caused by the disproportion of nitrogenous and non-nitrogenous elements (nitrogen and carbon) in food, that is, the amount of the nitrogenous was insufficient and that of non-nitrogenous excessive.

2. The symptoms of kakke patients are really due to these causes and the good results obtained by purgatives are due to their powers in getting rid of the abundant carbohydrates.

3. The pathological changes occurring in nerves, mucles, etc., are the results of inability of the tissues to repair the wastes, owing to the insufficiency of nitrogenous substances in the food, and the above changes are further aggravated by the presence of the large quantity of carbohydrates in the food.

In October, 1882, I submitted a proposal to the Minister of the Navy, the late Count Kawamura, the chief object of which was to change the dietary system existing then. When this proposal was put forward before a meeting there was a good deal of opposition.

They said that the change was too radical and instanced the great disturbances caused by the changes of diet in the Italian Navy some years before. They also called attention to the new system of fixing the amount of food by quality and quantity instead of by monetary value as in the old. In spite of difficulties caused by this opposition, my opinion finally prevailed, and the new system was decided to be adopted. But, as we required a few months longer in order to examine and fix the quality and quantity of food to be given, and as even some naval medical officers were holding the opposite view in heart, I took the opportunity of trying the new system on a certain number of kakke patients in the Tokyo Naval Hospital, comparing the result with that of the old system.

New Diet.

(1 Momme equals 58 grains Troy.)

Increased weight of 5 patients	1160 momme (9 pounds)
Decreased weight of 5 patients	360 momme (3 pounds)

The difference between the two is the increase of 800 momme (6 pounds), that is each person increased 160 momme (1.2 pounds.)

Old Diet.

Increased weight of 5 patients . . .	1340 momme (10.38 pounds)
Decreased weight of 5 patients . . .	490 momme (3.8 pounds)

The difference is the increase of 850 momme (6½ pounds), that is, each patient increased 170 momme (1.3 pounds).

Of the five patients experimented on with new diet, all were discharged with complete cure.

Of the five patients experimented on with old diet, four were cured and discharged from the hospital and one was changed into pulmonary disease.

As a result of these experiments it was found necessary to spend 36 sen 1 rin (about 17.5 cents) instead of 18 sen (about 8.5 cents) under the old system, that is, more than double.

In December of the same year an order was issued to make monthly statistics of body-weight of each person in the navy in order to ascertain the necessary amount of food for officers and men. By this means we got the following comparative scale of body-weight for five years, from 1884 to 1888.

In looking over Table IV, you will find that the body-weight is highest during the months of February, March and April and lowest in August and September. Therefore, after 1889 the weights were taken only in March and September, every year.

During ten years from 1884 to 1893 there was more or less difference yearly, but, taken as a whole, the weight has increased, that is, nearly eight pounds per person. From 1894 to 1903, for ten years, there was not much change in weight, and I think that shows the sufficiency of food supplied. During the former ten years the number of general diseases decreased in accordance with the yearly increase of weight. The last ten years showed not much change in weight and number of diseases.

Table IV shows that there was more or less increase or decrease even in a healthy body during twelve months and that these changes are physiological and have no relation to health.

On September 26, 1883, I, for the first time, spoke on the

cause of kakke before the meeting of the Japan Society of Hygiene and expressed my view as to the cause of the disease.

On October 5, 1883, I was promoted to be Director of the Medical Bureau.

Soon afterward, I asked the Minister of the Navy to have a special committee of investigation on the cause of the occurrence of the almost unprecedented number of cases of kakke on board the training-ship "Ryujo," which left Shinagawa on December 19, 1882, and returned to Shinagawa on October 15, 1883, after a voyage of 271 days to New Zealand, South America, and Hawaii.

My proposal was adopted and a special committee consisting of the following members was formed: *Chairman*, Rear-Admiral Maki, Surgeon-General Takaki, Captain Isobe, Commander Kunitomo, Fleet-Surgeon Kagami, Fleet-Surgeon Toyozumi, Paymaster Ijichi, Paymaster Kurihara, Secretary Iwamura, Lieutenant Serada, Clerks Matsumura, Sakamoto, and Mishina.

The first meeting of the committee was held on November 12, 1883. Chairman Maki explained the object of this committee and I was appointed the chief of the investigation board. After this, meetings were held five times a week, till April 11, 1884, and altogether the committee met seventy-nine times. During that time, seventy-six records were made, comprising 10,862 questions and 10,400 answers.

As a result, I, with the assistance of Staff-Surgeon Toyozumi, compiled ten reports concerning: (1) Patients, (2) clothing, (3) bedding, (4) food, (5) drink, (6) housing, (7) labor, (8) rest, (9) voyage, (10) anchorage, (11) weather and climate, (12) conclusion.

Besides, we made up six tables on diseases, thirty-two tables on food, one each on drink, climate, weather and temperature, and also tables on food supplied daily to petty officers, sailors, students, gun-room officers, and officers.

Finally the committee met on February 12, 1885, to discuss the results of investigations.

TABLE III.—*Average Monthly Body-weight of each Person from* 1884 *to* 1888.

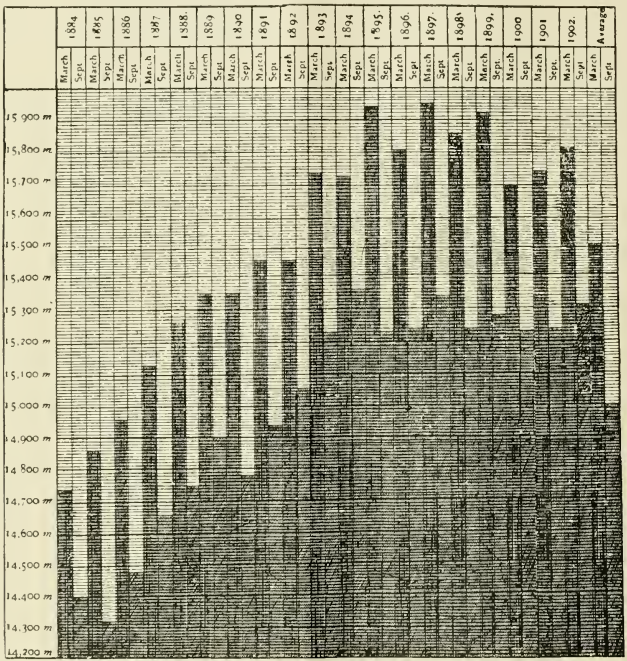

TABLE IV.—*Comparative Scale of Body-weight in March and September during Nineteen Years.*

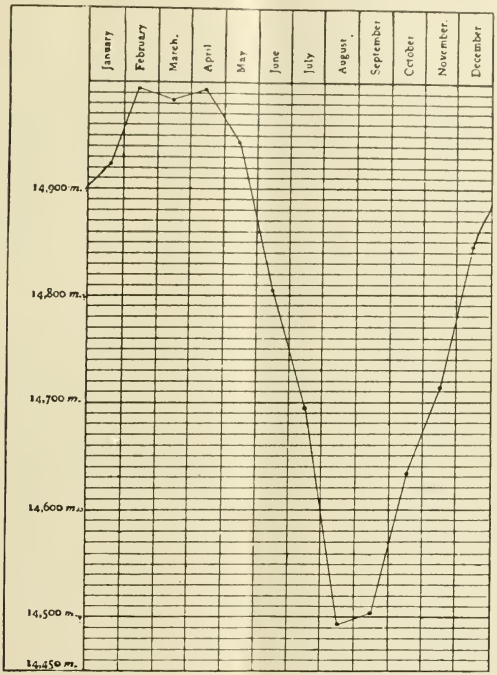

TABLE V.—*Average Daily Amount of Food for each Person during Nineteen Years from* 1884 *to* 1902.

Year.	Amount of food for each person per day.	
	Momme.	Ounces.
1884	606 63	75.83
1885	625.57	78.19
1886	644.62	80.51
1887	563.58	70.44
1888	551.13	68.89
1889	596.06	74.50
1890	443 01	55.37
1891	407.02	50.87
1892	399.56	49.94
1893	368.41	48.30
1894	416.08	52.01
1895	406.70	50.83
1896	384.90	48.11
1897	391.29	48.91
1898	406.75	50.84
1899	408 01	51.00
1900	415.45	51.93
1901	460.60	57.57
1902	438.55	54.82

In November, 1883, I was informed of the sailing of the training-ship "Tsukuba" in a short time and at once arranged to utilize this opportunity of testing the new system of diet by making her go the same route as that of the "Ryujo." So before the sailing of the Tsukuba, on November 24, 1883, I demanded the immediate practical application of the new diet, and in consequence, the Minister of the Navy issued the order to change the diet throughout the navy on November 29. Also on November 26, 1883, I proposed the necessity of the medical bureau having the reports on food supplied in ships, barracks, schools, etc., every month, and in the following December the Minister ordered this to be done. These reports have continued up to the present day.

The decrease of the amount of food since the year 1890 is due to the alteration of the food regulations in April of that year, and also to the fact that, according to the revised regulations, when members of a table company exceed five in number they are allowed to receive per every five members (this number was altered to ten in 1898 and resulted in a little increase of the amount of food since that year), one man's allotment in money, with which they can buy what ever food they like, and such food is excluded from the table.

Some increase of the amount of food from 1900 is also due to the alteration of food regulations from May of the same year.

The reason of decrease in the amount of nutritive elements since the year 1890, and that of some increase in it since the year 1898, is due to that stated in the note appended to Table V.

The present scale of diet supplied to the sailors is as follows:

On November 29, 1883, I had the honor of being presented to his Imperial Majesty at Akasaka Palace, and on this occasion explained my views as regards the cause of and preventive measures for kakke.

TABLE VI.—*Amount of each Nutritive Element in the Average Daily Amount of Food.*

Month.	Proteids.		Fats.		Carbohydrates.		Total.		Ratio of carbon to one of nitrogen.
	Momme.	Ounces.	Momme.	Ounces.	Momme.	Ounces.	Momme.	Ounces.	
January	38.93	4.86	8.45	1.05	160.40	20.05	207.78	25.97	16
February	38.21	4.77	8.52	1.06	160.19	20.02	206.92	25.85	16
March	38.00	4.75	8.34	1.04	159.88	19.98	206.22	25.77	16
April	39.08	4.88	8.89	1.11	161.72	20.21	209.69	26.20	16
May	37.91	4.74	8.38	1.04	170.89	21.23	217.18	27.01	17
June	39.19	4.89	8.56	1.07	163.95	20.49	211.70	26.35	16
July	38.79	4.85	8.67	1.08	160.74	20.09	208.20	25.92	15
August	37.85	4.73	8.58	1.07	157.72	19.71	204.15	25.51	16
September	39.39	4.92	9.11	1.14	163.87	20.48	212.37	26.54	16
October	38.41	4.80	8.68	1.08	160.83	20.10	207.92	25.98	16
November	38.65	4.83	8.39	1.05	162.74	20.34	209.78	26.22	16
December	38.85	4.85	8.54	1.07	162.96	20.37	210.35	26.29	14
Average	38.61	4.82	8.59	1.07	162.16	20.27	209.36	26.16	16

TABLE VII.—*Amount of each Nutritive Element in the Average Daily Amount of Food for the Period of Nineteen Years from* 1884 *to* 1902.

Year.	Proteids.		Fats.		Carbohydrates.		Total.		Ratio of carbon to one of nitrogen.
	Momme.	Ounces.	Momme.	Ounces.	Momme.	Ounces.	Momme.	Ounces.	
1884	52.17	6.52	11.67	1.43	206.16	25.77	270.00		16
1885	52.43	6.80	12.13	1.50	211.95	26.49	276.51		17
1886	56.73	7.09	12.86	1.60	204.66	25.58	274.25		15
1887	49.70	6.21	12.79	1.60	185.19	23.15	247.68		16
1888	48.57	6.07	11.78	1.47	177.38	22.17	237.73		15
1889	51.46	6.63	11.99	1.49	191.48	23.93	254.93		16
1890	42.44	5.30	7.75	0.94	147.44	18.43	197.63		15
1891	37.42	4.67	6.66	0.83	141.33	17.66	185.41		16
1892	38.74	4.84	7 33	0.91	144.79	18.10	199.86		15
1893	39.37	4.92	7.43	0.93	146.52	18.31	193.32		15
1894	42.23	5.28	8.04	1.00	160.79	20.10	211.06		15
1895	41.78	5.22	8.08	1.01	154.07	19.25	203.93		14
1896	39.53	4.94	7.64	0.95	145.52	18.19	192.69		14
1897	38.93	4.86	7.39	0.92	144.18	18.02	190.50		14
1898	45.37	5.67	8.05	1.00	143.40	17.92	196.82		17
1899	47.49	5.93	9 33	1.16	159.94	19.99	216.75		15
1900	48.75	6.09	9.79	1.21	158.24	19.78	216.78		15
1901	52.66	6.58	9.03	1.13	156.90	19.61	218.58		14
1902	38.61	4.82	8.59	1.07	162.16	20.26	209.36		16

TABLE VIII.—*Average Daily Amount of Food for each Person.*

Articles.	Momme.	Ounces.
Biscuit	8.95	1.12
Bread	52.97	6.62
Preserved meat	6.45	0.80
Preserved fish	6.50	0.81
Meat, fresh	53.98	6.74
Fish, fresh	19.60	2.42
Rice	100.49	12.56
Cracked wheat	34.26	4.28
Beans	3.44	0.43
Wheat flour	2.63	0.35
Dry vegetables	0.96	0.12
Vegetables	112.12	14.01
Tea	0.41	0.05
Baked barley	0.76	0.09
Sugar	9.91	1.24
Shoyu (a kind of soy)	19.89	2.48
Vinegar	1.52	0.19
Oil	0.54	0.07
Salt	1.83	0.23
Fat	1.30	0.16
Total	438.56	54.32

The Methods for Investigating the Cause of Kakke.

1. As we could not discover the true origin of kakke in spite of examination of symptoms, pathology, etc., we must use some other means.

2. In order to examine the food necessary for nourishing the human body, it is important to know the comparative scale of nutritive elements, that is, proteids, fat, carbohydrates and salts, and the proportion of carbon and nitrogen.

3. On examining the food taken by those suffering from kakke, it is found that the proportion of these elements is not correct.

4. The causes of this disease are due to the loss of equilibrium in the proportion of nutritive elements and also to the deficiency of a certain element; that is, the composition of food is not correct.

5. The occurrence of kakke due to the deficiency of a certain element, that is proteid, is shown in the examples of the long voyage of the "Asama," "Tsukuba," "Ryujo," etc. The disease does not occur if the food is well supplied:

for example, it does not occur among men having a sufficient supply of food or among officers, and in voyages with long stoppages at ports and short sailings. From 1882 to 1883, when the "Ryujo" went for long voyages, the disease disappeared completely as soon as she arrived at Hawaii, and was supplied with fresh articles of food.

6. High temperature, moisture, marshy air, overcrowding, hard labor, nervous exhaustion, coarse food, etc., cannot be considered the chief causes of kakke, because if they are the causes, both Europeans and Americans ought to suffer, but, on the contrary, they do not.

7. On considering the question both from theoretical and practical points, it seems quite reasonable, therefore, to suppose that the true cause of kakke lies in a wrong method of dieting.

In December, 1883, instead of the very simple rules of the previous years, I compiled a new book of instructions consisting of seventy-seven articles and twenty-two blank forms, and had it used throughout the navy with the approval of the Minister of the Navy. This book, since revised several times, is still in use.

On January 15, 1884, Jungi Kawamura, the Minister of the Navy, issued the following notification to the navy:

"It is hereby ordered that the following regulations in regard to the supply of food to the petty officers and men in ships and barracks shall be observed from February 1, 1884."

Regulations in Regard to the Supply of Food to the Petty Officers and Men in Ships and Barracks.

Article I. The food of petty officers and men in ships and barracks shall be under the control of the principal officer under whom they are serving, and the articles of food shall be bought with the money allotted for the purpose, and supplied to them.

Article II. The articles of food shall be as follows: Rice, bread, beef (fresh or preserved), salted beef, salted pork, fowls or eggs, fish, miso,[1] Shoyu (sauce), vegetables (potatoes, carrots, radishes, cabbages, and onions), beans, wheat flour, tea, fats, oils (suet or lard, butter, olive oil, oil of the sesamum orientalis), sugar (and starch), milk, vinegar, spices, alcoholic liquors, salt, pickles.

Article III. The articles of food shall be bought by the paymaster by order of the officer in command, and they shall be given out after being examined by the surgeon.

Article IV. A record of the articles of food shall be kept by the paymaster, which record shall frequently be examined by the officer in command.

Article V. If the preserved articles of food are found to be in bad condition, the matter shall be reported by the paymaster to the officer in command, who, in turn, shall order the surgeon or other officer to examine them and shall report the matter to the Minister of the Navy department, through the chief of different departments.

[1] A kind of sauce made of beans, barley, and salt.

TABLE IX.—*Daily Allowance of Food for One Healthy Person.* (*Fixed on the 24 of February*, 1884.)

	Momme.	Ounces.	
Rice	180.0	22 5	Bread 160 momme (20 ounces); biscuit 130 momme (16.25 ounces.
Meat fresh	80.0	10.0	When eggs are substituted, each egg to be reckoned as equivalent to 10 momme (1.25 ounces).
Fish fresh	40.0	5.0	Where there is no fish, 20 momme (2.5 ounces) of meat may be substituted.
Miso	14.0	1.75	
Shoyu	16.0	2.0	
Vegetables	120.0	15.0	
Beans	12.0	1.5	
Wheat flour	20.0	2.5	
Tea	2.0	0.25	
Fat or oil	4.0	0.5	
Sugar	20.0	2.5	
Milk	12.0	1.5	If condensed milk, 1½ momme (0.2 ounce) to be given.
Vinegar	2.0	0.25	
Spices	0.3	0.03	
Alcoholic liquors			This is in the case of Japanese liquors, and when other liquors are used, the quantity shall be fixed in proportion to the amount of alcohol contained.
Salt	2.0	0.25	
Pickles	20.0	2.25	
Fruit			To be given with care.
Total	568.3	71.00	

If the amount of 51 momme (6.37 ounces) of liquid food is subtracted there remain—

Momme.	Ounces.	
517.3	64.65	when rice is used.
496.3	62.30	when bread is used.
467.3	58.40	when biscuit is used.

It is not necessary to give the exact allowance every day, but if the food of two weeks is averaged, the average daily allowance should be equivalent to the daily prescribed amount.

In 1883, after my proposal to reform the diet system on November 26, I made a great effort to have the "Tsukuba" go over the same route as the "Ryujo." There was opposition to this from various points and the permission could not be obtained easily, but in the end, after much discussion, all difficulties were overcome except that of expense. So with the knowledge of the Minister of the Navy, I consulted Hakubun Ito, Councillor of the Imperial Household, and Seigi Matsugata, the Minister of Finance, and finally obtained my object by the special allowance of 60,000 yen (about $29,100) from the treasury.

Before the sailing of the "Tsukuba" a special committee for investigation was put on board, which consisted of the following gentlemen: Captain S. Arichi, Lieutenant Y. Matsumara, Surgeon T. Aoki, Paymaster N. Kataoka.

The food supply was ordered according to the new system. The vessel sailed on February 2, 1884, and returned to Shinagawa on November 16. The result obtained was good and is shown in Table X, comparing it with that of the "Ryujo."

When the good report ("no kakke") of the experimental voyage of the "Tsukuba" became known, the principal men in the navy for the first time began to support me in my fixed purpose.

They said that they had always opposed me in their hearts and only obeyed the new regulation because they were ordered by the Minister, but they would give in now after such powerful practical proofs.

In January, 1885, on looking through the reports of 1884, I was greatly satisfied with the results as shown in Tables I and II.

The number of general diseases was nearly halved and that of kakke considerably decreased, with no death.

On February 13, 1885, I made a new proposal for using barley and rice in equal proportions instead of rice alone, and of having this adopted from March 1, as the season of kakke was approaching, under the following rules, that is, from March 1 to March 15, only once at breakfast; from March 16 to 31, twice a day, morning and evening; after April 1, at every meal. I did this for the following reasons:

Although the number of cases of kakke in the navy decreased considerably (almost half the number in the year before) and the deaths had become almost unprecedentedly few since the formation of our navy, owing to these new food regulations of February, 1884, yet the disease had not yet

TABLE X.—*Comparative Table Showing the Duration of Voyage and of Stay in Port, State of Weather, Amount of Food, and Number of Cases of Kakke during the Voyages Made by the "Ryujo" and "Tsukuba" to South America.*

Period.	Date.	Voyage.	Duration of voyage or stay. (Voyage of "Ryujo" 1882–1883).	Days.	Temperature. (Fahr.)	Barometer.	Weather.	Days.	Daily amount of food taken by one person.	Momme	Cases of kakke.
First period	Dec. 19, 1882, to Jan. 31, 1883	Shinagawa to Wellington	Voyage	44	66-87	29.75-30.19	Clear	16	Animal	25.57	3
			Stay	...			Fair	17	Vegetable	351.97	
							Cloudy	8			
							Rain	3			
Second period	Feb. 1, 1883, to Mar. 31	Wellington to Valparaiso	Voyage	44	67.5-74	29.98-33.26	Clear	11	Animal	37.63	7
			Stay	15			Fair	25	Vegetable	276.70	
							Cloudy	15			
							Rain	8			
Third period	April 1 to May 31	Voyage continued; stay at Valparaiso; to Callao; stay at Callao; to Honolulu	Voyage	39	67.5-79.7	27.62-30.16	Clear	29	Animal	38.07	25
			Stay	22			Fair	16	Vegetable	290.89	
							Cloudy	13			
							Rain	3			
Fourth period	June 1 to July 31	Voyage continued; stay at Honolulu	Voyage	32	81.5-83.8	29.99-30.18	Clear	47	Animal	61.68	125
			Stay	29			Fair	13	Vegetable	279.99	
							Cloudy	6			
							Rain				
Fifth period	Aug. 1 to Sept. 15	Stay at Honolulu; to Shinagawa	Voyage	42	81.8-86.0	26.30-33.56	Clear	1	Animal	69.95	
			Stay	4			Fair	34	Vegetable	223.28	
							Cloudy	5			
							Rain	1			
Total	271 days		Voyage	201	Max. 87	Max. 33.56	Clear	104	Animal	12,622.18	160
			Stay	70	Min. 66	Min. 26.30	Fair	105		46.58 oz.	
							Cloudy	47	Vegetable	77,118.47	
							Rain	15		284.79 oz.	
		Voyage of "Tsukuba" (1884).									
First period	Feb. 3, 1884, to Mar. 31	Shinagawa to Auckland; stay at Auckland	Voyage	48	63-98	30.98-30.13	Clear	24	Animal	125.59	5
			Stay	9			Fair	16	Vegetable	363.12	
							Cloudy	10			
							Rain	7			
Second period	April 1 to May 31	Stay at Auckland; to Valparaiso	Voyage	41	69-74	29.89-29.98	Clear	29	Animal	125.91	7
			Stay	20			Fair	20	Vegetable	351.43	
							Cloudy	10			
							Rain	2			
Third period	June 1 to Sept. 31	Voyage continued; stay at Valparaiso; to Coquimbo; stay at Coquimbo; to Honolulu	Voyage	30	68-70	27.71-30.86	Clear	31	Animal	114.66	1
			Stay	31			Fair	13	Vegetable	342.62	
							Cloudy	12			
							Rain	5			
Fourth period	Aug. 1 to Sept. 30	Voyage continued; stay at Honolulu	Voyage	50	74-83	27.99-32.97	Clear	30	Animal	114.87	3
			Stay	11			Fair	15	Vegetable	308.83	
							Cloudy	13			
							Rain	3			
Fifth period	Oct. 1 to Nov. 16	Stay at Honolulu; to Shinagawa	Voyage	39	75-84	33.37-29.68	Clear	17	Animal	126.88	
			Stay	8			Fair	12	Vegetable	324.88	
							Cloudy	16			
							Rain	2			
Total	287 days		Voyage	208	Max. 98	Max. 33.37	Clear	131	Animal	34,893.46	16
			Stay	78	Min. 63	Min. 27.71	Fair	76		121.50 oz.	
							Cloudy	61	Vegetable	97,017.48	
							Rain	19		338.04 oz.	

disappeared completely and we were obliged to make further efforts to exterminate it. Then I thought of the plan of using barley instead of bread alone as the men could eat the former better than the bread. From this, I expected better results. The Minister of the Navy ordered the addition of the word "barley" among the articles of food and its practical application on December 21, throughout the whole navy. As I saw uneasiness arising among the naval officers and men, owing to this change, and as I wanted to report the full results of the investigation on the voyage of the "Ryujo" and to tell the purpose of this new change, I, with the approval of the Minister of the Navy, delivered the following address at the Naval Club on February 25, 1885:

"All of the gentlemen here present will remember the Orders G. No. 2743 (2), issued on November 29, 1883, and C. No. 7, issued in January, 1884, by which regulations regarding food were made for the first time. By last year's experience, we have found that most of the men dislike meat as well as bread, and we do not know what we shall do next. But if we leave the matter to their own choice, we shall certainly have a great many cases of kakke, as has hitherto been the case, especially as more than 1000 new men have been enlisted this year. Now, there is nothing better than barley food for preventing kakke. As, however, barley is coarse in appearance, we are afraid that some of the men who do not understand the object of the improvement in the scale of diet will feel dissatisfied. We consequently wish to speak about the preventive measures to be adopted against kakke and to take this opportunity of reporting the result of the examination into kakke on board the 'Ryujo.'

"That kakke can be prevented by an improvement in the scale of diet has been deduced from scientific reasoning, and has been proved by experience in our navy, and for a long time we were planning such preventive measures. Fortunately, G. No. 2743 (2) was issued on November 29, 1883, directing that nutritious food should be given as far as possible to which followed the regulations in regard to the supply of food, which were issued with C. No. 7, in January, 1884. According to those regulations, the Medical Bureau drew up tables showing the proper amount of food for healthy men and invalids, thus trying to insure the health of the men. As we had expected, however, these suggestions often could not be carried out, especially in the case of newly enlisted men, who not only dislike bread, but cannot take a proper amount of meat. If things are left in such a condition, there is no doubt, from recent experience, that we shall again have a great many cases of kakke this year, in spite of the favorable result shown in the decrease of cases of kakke which was obtained in the year which followed the improvement in the scale of diet. This is why we decided to give the barley food. We believe that the majority of the men in our navy have been used to take barley food from their childhood, so that in reality they can eat it, although they show their dissatisfaction at it after becoming accustomed to the rice given to them since they entered the navy. It is accordingly considered that the best preventive measure, at present, against kakke, will be to give barley, which it was directed should be given to the navy in general, from the month of March, by the order of the 21st. If this order is carried out strictly, we are sure to find no case of kakke in our navy. We consequently ask you gentlemen, that you will kindly help us in the work of prevention, for the good of our country, according to the order just given."

On March 19, 1885, I obtained the honor of an interview with His Majesty the Emperor, and presented the reports of the following items:

1. The results of kakke investigation on board the "Ryujo."

2. The decrease of kakke from the gradual improvement of diet since January 15, 1884.

3. A great probability of exterminating the disease from the navy in a few years.

On March 28, 1885, I, for the second time, spoke on the preventive measures of kakke before the meeting of the Hygienic Society of Japan, the chief items of which were:

1. The report of the investigation committee placed on board the training-ship "Ryujo" during its voyage in 1883.

2. The report of the experimental voyage of the "Tsukuba" in 1884.

3. The results obtained through the examination of food supplied in 1883, that is, the very small quantity of nitrogenous food as against the large amount of carbohydrates, the proportion being 1 part of nitrogen to 28 parts of carbon.

In addition the occurrence of numerous cases of kakke and general diseases during that year.

4. The good results obtained by improved diet since 1884 and the difference brought about in the proportion of nitrogen and carbon by various changes in the proportion of diet.

On August 24, 1885, I made a proposal to change bread and biscuit for equally proportioned barley and rice which had been supplied since March of that year, because I recognized its necessity owing to the great difficulties in cooking during rough weather, even in time of peace. In November of that year my proposal was taken up and its application was at once ordered.

Beside, arranging and investigating as described, I had thought of experiments on dogs, and in September, 1884, commenced my experiments. The results obtained were as follows:

1. *Experiments on Dogs.*

I took six dogs at the beginning of September, 1884, and separated them into two groups, A and B, and fed them with different combinations of food materials.

The dogs in Group A received a diet consisting principally of rice and other vegetables, while those in Group B received also a considerable amount of fresh beef daily, besides rice and vegetables.

The Result. No. 1 of Group A, in a short time, increased 100 momme in his weight, but later gradually losing weight, became thin and weak; moreover, his hair had fallen very much, but he did not show any symptom of disease. However, he died suddenly on the morning of July 21, 1885. On comparing his weight when he died with that first taken he had lost 400 momme. He was reared for a period of 307 days.

Postmortem Examination. Every part of his body showed indications of anemia, his heart and veins being markedly congested. A great many filariæ were found in the heart and veins, and besides, under microscopic examination, it was ascertained that there were some very minute filariæ in the blood.

No. 2 of Group A increased his weight for a short time, *i. e.*, 10,760 momme, but soon after begun to waste gradually. On comparing with the weight first taken he still showed an increase of 735 momme. Notwithstanding the increase in weight he died on the two hundred and sixty-ninth day after the commencement of the experiment. The symptoms of the illness and result of postmortem examination were as follows:

Since May 12, 1885, he was averse to taking food; after six days he took almost nothing; and from about May 22 his strength became greatly diminished and he could not frisk about as formerly, the corneæ became dull, tears running down continuously, and he became very much emaciated. On May 25 his hind legs became paralyzed and he could not walk. He could not feel the prick of a needle on his skin. The blood from the mucous membrane of his mouth was taken and cultured without any result. After that his hind legs became more and more paralyzed, and at last the paralysis extended to his forelegs so that he could not stand. He died on the night of June 5. On the day following, postmortem examination was made and every part of the internal organs was found anemic. The brain and spinal cord were soft and in the right side of the heart there were many threadworms, about seven or eight inches long, and a great many filariæ sanguinis hominis were found in the blood.

No. 3 of Group A for a short time increased in weight to 2660 momme and after that the weight gradually decreased, but comparing it with the weight first taken it still showed an increase of 610 momme. Still, in spite of the increase, he died after three hundred and thirty-seven days' rearing.

The symptoms and results of the postmortem examination were as follows:

Since August 15, 1885, his body became emaciated and he could not frisk about as usual. His left eye became ulcerated, dark, and very much contracted; on August 19 both his forelegs and hindlegs became paralyzed and he could not walk. For a trial, his forelegs were pricked with a needle and he seemed to feel some pain, but his hindlegs had entirely lost sense of feeling. He died on the night of the same day.

Postmortem Examination. Brain, spinal cord, kidneys, and right lung were full of blood; intestines, stomach, liver, heart, left lung, and rest of the body showed a deficiency of blood. In the latter no unusual change was detected.

No. 1 of Group B lost weight at the beginning, but afterward gradually regained it. When compared with the weight first taken it increased 180 momme, and after the lapse of three hundred and seven days he was still healthy and strong.

No. 2 of Group B, from the beginning, increased in weight to 4540 momme and after that gradually decreased but when compared with the weight first taken it still showed an increase of 2030 momme and after the lapse of two hundred and sixty-one days he was healthy and strong.

No. 3 of Group B lost weight as much as 780 momme, when compared with the weight first taken, but after the lapse of three hundred and thirty-seven days he was still healthy and strong.

The increase in weight of three dogs of Group A, when compared with the weight first taken showed an increase of 2995 momme, but all the dogs died.

The total increase in weight of three dogs of Group B, when compared with the weight first taken, was only 1430 momme, but all were still alive and healthy. Therefore, it is not always reasonable to take the increase of bodily weight as a positive proof of health.

The above results are proofs of the difference in the physiological constitution of animal life produced by the consumption of different combinations of food. It is also shown by the quantity of feces passed, that the digestion and absorption are not the same in each dog, though the same combination of food is given to each. Further, the quantity of excrement of those dogs which took the food mixed with meat is less than that of the dogs which took no meat. It is not worth mentioning more details of the above.

2. *Experiment on Dogs.*

This experiment was commenced on September 1, 1885, and completed on November 30, 1886.

At this time, as at first, six dogs were used and separated into two groups, A and B, and differently combined foods were given to each group.

The principal articles of food given to Group A were rice and sweet potatoes, and that given to Group B consisted

of boiled barley, beans (soja hispidia), and sweet potatoes. The other articles of food given to each group were the same and the quantity of these articles was determined according to the weight of each dog.

The Result. A summary showing the number of days over which the experiment extended and the results of the experiments is shown in the following remarks:

No. 1 of Group A during the first period (duration of a period is one month) decreased slightly in weight, but since then increased more or less. During the ninth period the increase reached its highest point (one-eighth of its original weight), but the decrease followed during the tenth period when the weight reached its lowest point and during the thirteenth period the dog died.

During the time between the sixth and twelfth periods and at the time when it died spasms took place. The experiment extended over three hundred and eighty-three days.

Postmortem Examination. The body was not much emaciated. In the abdomen there was one ounce of liquid, its color being light yellow and transparent; there was slight congestion and hemorrhage in the peritoneum, stomach, and intestines, but there was no other abnormal change in the other viscera. There were six ounces of fluid in the right side of the chest and one ounce in the pericardium; there was slight congestion in the posterior part of both lungs; one of the tricuspid valves of the heart was thickened and congested, and owing to its adhesion to the ventricular septum causing marked regurgitation. No filariæ were found, also no œdema. Microscopic examination did not disclose anything unusual.

No. 2 of Group A decreased slightly in weight during the first period, and it increased a little during the second period, but since then the weight at each period up to the seventh, when compared with that of the first period, showed a decrease. However, during the eighth period it again increased and at the commencement of the ninth period it reached the maximum, showing an increase of nearly one-eighth of its original weight. After that the weight rapidly decreased and during the eleventh period the animal died. From the commencement of this period she showed signs of ill-health and often refused to take food; then the weight gradually decreased, and the animal became emaciated, haggard, and averse even to walking. From the seventh day of this period her breathing became gradually hurried and she coughed continuously but without expectoration.

Henceforward the coughing increased very much and the animal became extremely weak; she could not endure a long walk and on the nineteenth day she died, but no sign of paralysis was observed. The experiment lasted three hundred and twenty-two days.

Postmortem Examination. Thin and bony, chest and belly swollen, and in the abdomen there were three and one-half ounces of yellowish, transparent fluid; the small intestines were slightly congested, and there was hemorrhage in the mesentery and mucous membrane of small intestine, but no change in other viscera. There were seventeen and one-half ounces of fluid in the right chest and sixteen and one-half ounces in the left chest, but practically none in the pericardium; there was no visible change in the pleura and the lungs did not contain much air; the base was destitute of air and its portions cut off sunk in water, but no tubercular deposit was observed. There were five filariæ in the heart.

No. 3 of Group A at the end of the first period weighed the same as at the very beginning, but at the seventh period the weight suddenly increased and reached the maximum point. After that it sometimes increased and sometimes decreased, but the weight of each period compared with that at the very beginning showed more or less increase, and it continued to keep up an increase of 20 momme till the end. Generally speaking, this dog passed the whole period of the experiment without much change in weight or in other respects. This dog was reared for four hundred and twenty-one days.

No. 1 of Group B lost much weight in the first period, and at the beginning of fourth period lost over one-quarter of his original weight. However, his movements were very active though he was slightly emaciated, but he showed signs of recovering his weight during the ninth period, and comparing it with that of the beginning showed slight increase; after that, increasing at every period it reached its highest point during the twelfth period, and then again decreased. But on comparing the decrease with that of the first period it still showed an increase of 150 momme. The experiment was carried out for four hundred and fifty-six days.

Although No. 2 of Group B increased in weight during the first period, yet later on it decreased more or less except during the eighth period, then it again increased a little. From that time it continued to increase more or less at every period and at the expiration of the experiment it still kept up an increase of 120 momme. This dog continued the whole length of time without remarkable change in its weight, and nothing unusual happened. During the fifth and sixth periods the weight decreased, but again increased during the seventh period; since then it increased more or less during every period. At the end it showed an increase of 140 momme. The period of experiment was four hundred and fifty-six days.

As is mentioned above, No. 1 and No. 2 of Group A during the ninth period attained the highest point of weight, and though they increased one-eighth of their original weight after a short time, yet they decreased again and the animals died.

No. 3 of Group A lived (experimental period), and though increased in weight the increase was not more than 20 momme.

Although the three dogs of Group B lost weight considerably for a short time, yet during the last period each of them increased in weight and at the end of the experiment the increase was from 120 to 150 monme.

An important thing to be noticed is the difference in quantity of urine and feces between Groups A and B. On comparing them A's is the lesser, and the probable cause of this is that the digestion of barley is considerably inferior to that of rice.

The result of the two experiments mentioned above was that those six dogs to which rice was given as the principal food, in spite of an increase in weight, all but one died (before the expiration of the experiment).

The increase of weight of six dogs to which barley, beef, and beans were given as their principal food was not so conspicuous as in that of Group A, but every one of them was healthy and very active both mentally and bodily, till the end of the experiment.

Therefore, although these experiments seem to be very crude yet the results certainly prove that the variety of food consumed and its combination have direct influence upon the health of animal life.

It is not quite proper to conclude that the causes which affect the health and development of man will produce in some ways the same results as in dogs, but I have no doubt that the health of man is also greatly influenced by the variety and combination of food consumed.

By the beginning of 1890 the reformed diet was crowned with a complete success, and not only was kakke wholly exterminated, but also the general diseases became greatly decreased.

In the same year the Imperial ordinance for the reformed diet was issued and thus my original object was fulfilled.

All through these years of hardships I tried to explain my views to others by comparing the food to gunpowder. I said that the former is the primary force of the human body, as is the powder in the case of the gun, so it is just as important to select the food suitable for sailors as the powder for guns and rifles.

In former years the food was supplied according to the monetary system without any regard for quality or quantity. Therefore, when the price of food articles was high the men could not get sufficient nutrition for the maintenance of health, although they were able to get more when it was low. As a consequence, the distribution of food was unequal at times, and although the sailors could stand any hardships at one time, yet they could not at other times, owing to the want of food. Such a state of things is a serious danger for the country in time of need. The gunpowder is supplied in definite quantity and of the best quality without considering the amount of expense. This is what I wished to have with regard to the supply of food. By doing so we can preserve an equal supply of suitable food at all times and also keep the officers and men in good health, so that they can bear hardships both in peace and in war. In 1890, as the success of the reformed diet became positive, the particulars concerning the preventive measures taken for kakke were compiled into a book and presented to the Minister of the Navy.

As the result of the reformed diet and the improvement of the naval hygiene, during six years from 1884 to 1889, the amount of expense saved totalled 1,232,416 yen (about $597,725). On October 16, 1890, I, for the third time, had the honor of an audience with His Majesty the Emperor and presented the following facts:

1. As I foretold on the occasion of the presentation to His Majesty in 1885, kakke had now been completely exterminated from the Imperial Navy.

2. The present condition of the health of the Imperial Navy and the economic influence of the improved diet.

3 The fear of the inability of the naval officers and men to endure hardships in time of need had now gone.

4. The general tendency of kakke to increase among students and others without any regard to occupation.

5. The appearance of kakke all over the country and its tendency to increase seemed to have its origin in the reformed land tax of the sixth year of Meiji (1873). Since that time the habit of eating rice as the chief food settled upon the remote districts; and besides, owing to the general tendency throughout the country to raise mulberry leaves, the production of rice and other cereals markedly decreased. In consequence, the vegetable albuminates contained in food necessary for bodily nutrition decreased, while on the contrary the amount of carbohydrates comparatively increased, thus causing the increase of the disease.

On thinking over my past experiences I cannot hesitate to declare that the present improved condition of the Imperial Japanese Naval hygiene was due to having had an able man at the head of the navy and also to the education of medical officers. Because if we had not such a man at the head my suggestions would not have been taken up, or if the medical officers were not thoroughly educated they could not have succeeded in the task of the preventive measures. The success of the new diet system and the attaining of my long-cherished desire were accomplished owing to the late Count Jungi Kawamura, who was the Minister of the Navy when I was made the Chief Director of the Medical Bureau. When I first took up official duty as the Director of the Medical Bureau I told the Count that if he would give me full power to execute whatever I deemed necessary in order to keep up the health of the naval officers and men, so as to make them fit for any duty, I would endeavor not to interfere with his plans (in regard to education, training, duties of officers, and men). These plans, it may be mentioned, seemed to

be throwing too much work on the men, and medical officers were inclined to object. He then answered "All right." So that whenever I wanted to try any new plan, he always supported me in carrying it out as long as circumstances allowed.

In order to maintain the health and efficiency of the men I firmly believe it to be of paramount importance to have the following facts in constant observation:

A careful selection of men at the time of enlistment and the maintenance of their health are absolutely essential for the object of having an army and navy.

To fulfil these objects there must be an organization in which the medical officers and nurses must be properly educated so as to fit them for their duties, and the officers and men of other branches must be taught elementary physiology and hygiene. Accordingly in Japan elementary physiology and hygiene are taught to cadets and officers, in addition to the subjects special to themselves, both at the Naval College and the Academy.

The influence of the sanitary precautions on the death-rate in the navy, following severe engagements, is shown in the following tables, giving the reports from the beginning of the war between Japan and Russia until December 5, 1905:

TABLE XI.—*Total Number of Casualties in Action with Results in Japan–Russian War Ending December 5, 1905.*

Classification.	Total number of killed and wounded.	Killed outright.	Subsequently died.	Survived wounds.	Cured.		Remaining.	
					Returned to duty.	Invalided.	In hospital.	Out.
Officers	307	159	14	134	132	...	1	1
Gun-room officers	93	51	4	38	37	1		
Petty officers	891	511	27	353	319	27	7	
Men	2333	1139	68	1126	1010	74	42	
Miscellaneous	65	31	4	29	23	...	1	
Total	3689	1891	117	1680	1521	102	51	1

Percentage of death-rate, including subsequently died, is	54.0 per cent.
Percentage of instant death.	51.0 "
That of returning to duty after wounded	90.8 "
That of invalided	6.0 "
In hospital	3.0 "

TABLE XII.—*Total Number of Deaths in the Battle Outside Port Arthur, February 9, 1904.*

Classification.	Total number of killed and wounded.	Killed outright.	Subsequently died.	Survived wounds.	Cured.		Remaining.	
					Returned to duty.	Invalided.	In hospital.	Out.
Officers	16	2	1	13	13			
Gun-room officers	2	...	1	1	1			
Petty officers	11	1	1	9	9			
Men	42	—	3	39	35	3	1	
Miscellaneous	1	...	...	1	1			
Total	72	3	6	63	59	3	1	

TABLE XIII.—*Total Number of Casualties in the Battle at Yellow Sea, December 10, 1905.*

Classification.	Total number of killed and wounded.	Killed outright.	Subsequently died.	Survived wounds.	Cured.		Remaining.	
					Returned to duty.	Invalided.	In hospital.	Out.
Officers	28	12	1	15	15			
Gun-room officers	6	3	...	3	3			
Petty officers	64	29	3	32	28	4		
Men	127	21	2	98	80	18		
Miscellaneous	7	...	...	...	...	...		
Total	232	65	6	155	133	22		

TABLE XIV.—*Number of Casualties in the Battle at the South Eastern Coast of Corea.*

Classification.	Total number of killed and wounded.	Killed outright.	Subsequently died.	Survived wounds.	Cured.		Remaining.	
					Returned to duty.	Invalided.	In hospital.	Out.
Officers	9	1	1	7	7			
Gun-room officers	2	...	...	2	2			
Petty officers	35	13	3	19	18	1		
Men	83	22	6	55	49	4	1	
Miscellaneous	4	...	...	4	4			
Total	133	36	10	87	80	5	2	

TABLE XV.—*Number of Casualties of the Men for the Siege of Port Arthur.*

Classification.	Total number of killed and wounded.	Killed outright.	Subsequently died.	Survived wounds.	Cured. Returned to duty.	Cured. Invalided.	Remaining. In hospital.	Remaining. Out.
Officers	6	1	2	3	3			
Gun-room officers	8	3	1	4	4			
Petty officers	61	6	4	51	44	7		
Men	268	20	20	228	205	22	1	
Miscellaneous	...	...	...	...	...	...	...	
Total	343	30	27	286	256	29	1	

TABLE XVI.—*Number of Casualties in the Battle of Japan Sea, May 27, 1905.*

Classification.	Total number of killed and wounded.	Killed outright	Subsequently died.	Survived wounds.	Cured. Returned to duty.	Cured. Invalided.	Remaining. In hospital.	Remaining. Out.
Officers	49	5	2	42	40	...	1	1
Gun-room officers	14	2	...	12	12			
Petty officers	158	34	3	121	112	2	8	
Men	469	45	22	402	358	8	36	
Miscellaneous	10	2	2	6	5	...	1	
Total	700	88	29	583	527	10	45	1

TABLE XVII.—*Number of Casualties in the Time between February 9, 1904, up to August 13, 1905, Excluding the Big Battles.*

Classification	Total number of killed and wounded.	Killed outright.	Subsequently died.	Survived wounds.	Cured. Returned to duty.	Cured. Invalided.	Remaining. In hospital.	Remaining. Out
Officers	199	138	7	54	54			
Gun-room officers	61	43	2	16	15	1		
Petty officers	562	428	13	121	108	13		
Men	1350	1031	15	304	283	19	2	
Miscellaneous	43	30	2	11	11			
Total	2215	2670	39	506	471	33	2	

REMARKS. The percentage of "killed" in the navy was, as is seen in Table XI, 51 per cent., while that in the army was 28 per cent., thus showing that the "killed rate" is much larger in the navy. This is no doubt due to the more powerful weapons used in the navy, which cause great damage from explosive shells.

All the wounded cases have been aseptically treated under strict observation, and, of course, when the necessity arose cases were treated antiseptically according to the nature of each case. Surgical operations were generally avoided as much as possible because it was found that conservative surgery gave the best result.

In our army and navy, before the battle commences, we are in the habit of wearing new clothes after cleansing the body thoroughly, as a matter of self-respect, and this is also useful as a preventive method against the introduction of any infection from the outside when a man is injured or wounded.

MILITARY SANITATION

On the subject of the army sanitation, I am afraid I cannot quite claim the same knowledge, and speak with the same authority as in the case of the navy, owing to the fact that my duty was chiefly concerned with the navy. As to the practical experiences I can claim only very little which I acquired during my short stay in Manchuria. But the English army had a most capable man at the front as its Military Attache, and Lieutenant Colonel W. G. Macpherson, R. A. M. C., the late British Military Attache to the Japanese Army, has already described and published articles concerning our medical organization for the preservation of the health of the army under the title of "The Medical Organization of the Japanese Army," in the journal of the *Royal Army Medical Corps*, March, 1906. If any of you are interested in the subject of our medical organization I strongly recommend you to read his clear and excellent article in that journal. The facts are very clearly and correctly described, and I think you may rely on them without fear. The time at my disposal being short, I will omit the subject of our medical organization, and will proceed to explain various figures, which I obtained from our military authority in Tokio, showing the results of our efforts in the preservation of the health in the army. The struggle against kakke which has been going on in the navy has also been taking place in the army, and the percentage of kakke cases was a good indication of the general health of the army, because whenever kakke cases diminished, the health of

the army also improved generally—that is to say, cases of other diseases decreased proportionally.

The health of our army has been gradually improving in late years, but kakke is not yet eradicated as it is in the navy, and I regret to state that although the cases are few in time of peace at home, the disease is apt to break out in time of war just at the time when stronger men are needed. In former years kakke prevailed largely in the army as it did in the navy, but now it occurs less frequently than before. The following table explains the facts:

Kakke per 1000 *Men.*

Name of division, etc.	1883	1884	1885	1903
Imperial guards	489.53	486.56	269.82	
Gendarmes	408.17	354.54	254.96	
Academy, etc.	607.70	735.00	412.12	
School of sergeants, etc.	217.82	412.89	349.81	
Tokyo division	349.38	467.99	311.16	
Sendai	120.16	216.02	138.36	14.63
Nagoya	119.55	100.24	94.58	
Osoka	308.31	232.90	7.07	
Hiroshima	144.82	2.85	3.08	
Kumamoto	102.95	154.75	89.17	

This table shows that the disease was violent in its attacks. The different sections of the army suffered differently as to numbers, so that the hospitals provided for certain divisions were inadequate to take all the cases of kakke; therefore, in order to meet such emergencies, other accommodations were provided in the special localities to which patients could be sent, such change of air being considered beneficial and curative.

The Nagoya Division. The number of kakke cases greatly diminished in 1885. This result is considered to have been due to a supply of rice with barley in proportion of 7 to 3. The Hiroshima division has suffered very little in general. The price of food is less there than at other places, so that better and more nutritious food could be supplied at the same expense, and therefore the division was supplied with some bread in place of rice. The results of the experimental use of barley in the Osaka division and navy induced the army authorities of other divisions to adopt a supply of barley in proportion of 3 of barley to 7 of rice, and the result in 1903, as shown by this table, was a decrease of kakke.

Unfortunately, during the Chino-Japanese and the beginning of the Russo-Japanese wars, owing to circumstances, only rice was given to the men as principal food, and as a consequence cases of kakke increased greatly, in fact, there being a very much larger number of cases than usual. But in the later period of the Russo-Japanese war when we began to give the men barley with rice and increased the quantity of meat the cases of kakke decreased rapidly with this change in diet. Another illustration of the influence of diet upon the health of the men is shown by the fact that there was not one case of kakke among the sailors of the naval brigade during the siege of Port Arthur, although there was a large number of kakke cases in the army. These men lived among the soldiers and under exactly the same conditions, but they differed from the soldiers in one respect, that they were supplied with one pound of meat, ten ounces of barley, and thirty ounces of rice per day, while the soldiers were supplied with five ounces of meat and thirty ounces of rice per day. The above examples confirm my view that kakke largely occurs among men who are fed with an insufficient quantity of nitrogenous food and an excess of carbohydrates.

From the reports received until June 30, 1905, concerning troops in Manchuria, and until the end of August, 1905, concerning troops in Corea and Saghalin, the proportion of officers killed to officers wounded is as 1 to 3.25, and that of non-commissioned officers killed to wounded is as 1 to 3.56. The proportion of deaths from wounds including both killed and those dying subsequently from wounds is as 1 to 3.94. The proportion of deaths from infectious diseases and diseases from all causes to that of death from wounds is as 1 to 4.

From the reports received from the beginning of the war until the end of August, 1905, the total number of patients located in the army is 281,547, and the proportion of wounded to cases of infectious diseases and general diseases and accidents is as 1.0 to 1.5. The total number of cases of kakke occurring in the army during this time is 97,572, with 3756 deaths.

The preceding reports are of great interest in showing the progress that has been made in our army in the preservation of health since the Chino-Japanese war. Comparing the result of the Chino-Japanese war with that of the recent war against Russia we find the following facts:

1. That cholera has practically disappeared.

2. That typhoid fever cases decreased from 37.14 per thousand men to 9.26 per thousand. The death-rate therefrom is almost halved.

3. That dysentery cases decreased from 108.96 per thousand of men to 10.52 per thousand. The death-rate was brought down from 15.72 per thousand men to 2.68 per thousand.

4. That malaria cases decreased from 102.58 per thousand men to 1.96 per thousand. The death-rate is practically nil.

These remarkably good results were chiefly the results of the progress made in the medical organization as regards food, drink, clothing, camping-ground, etc., and we took particularly great pains to exterminate flies and to prevent them from coming in contact with the body, the articles of daily use, and into the dwelling houses. Nets were used at windows and doors of the houses in order to prevent flies from coming in, and also to protect the exposed part of the body, such as the face, when flies were in abundance. The extensive use of muslin nets against flies and at the same

time against mosquitoes may possibly be responsible, besides the improved sanitary organization, for the remarkable decrease in the number of typhoid, dysentery, and malaria cases. I may mention that another prophylactic, which we did not employ previously, was the use of creosote pills. Each man in health was supposed to take one of these daily, throughout the campaign; and this, too, may have had some influence in causing these improved health conditions.

GENERAL REMARKS

During the recent war we had to take the most strict precautions to keep our men free from any epidemic disease by the carrying out of various plans arranged at the beginning of the war. For instance, as to the supply of water, we had to provide a water cart drawn by four horses and a water boiler cart drawn by one horse, and boiled water stations were established and a small mess tin was carried by each soldier, so that he could have boiled water by boiling it in his own mess tin when the necessity of doing so arose. At the boiling water station during the march the soldiers had to fill their own water bottle with boiled water. During the march when they had exhausted their own water bottle they had to get water from the water boiler cart which always accompanied the troops when possible and necessary, and the water carts were almost always with them. When they had to get water from a stream or river, they were ordered to get the drinking water from the centre of the stream so as to avoid the impurities coming from the bank of the rivers; even then the water had to be boiled before they took it. As a result of experience they found some difficulty in knowing whether water which they got during the night was pure or dirty. They could, of course, see the water, but the light was not sufficient to enable them to say whether it was pure or not. We had to take great care during night marches.

Food. Almost all foods were sent from Japan to the front under strict superintendence of officials who ranked as officers, but, of course, whenever they could they obtained fresh food locally, took strict precautions not to get any injurious materials from the natives, because there was some danger of poisons being mixed with them. We therefore tried our best to give fresh food as much as possible. During the severe winter the soldiers had to keep their mess tin wrapped in a piece of flannel and keep it under the overcoat, so as to prevent its freezing. They also were ordered to cook their rice, each time they had to eat it, according to the circumstances, and also at times they were given biscuit in place of rice and barley. During the hottest part of the summer they added a small quantity of acetic acid to the cooked rice and barley in order to prevent decomposition. Besides a regular supply of food materials, the soldiers were allowed to buy some eatables locally according to special regulations laid down, prohibiting them from buying food directly from the natives. Sake, two ounces on an average, was allowed to each as an extra, under strict superintendence of the medical officers. Sweets were allowed to those who had no inclination to drink sake.

Camping. Whenever they had to go into camp, first of all a party, so-called camping party, consisting of the line and medical officers, was sent out to select a place where they could be safe, from a strategical and from a sanitary point of view, and medical officers had to inspect the source of water supply, the condition of houses found there, and the people living therein. When medical officers found any water which was unfit to drink, they put up a notice cautioning the troops not to take it, and in case where there was great liability for the soldiers to take it, according to circumstances, they had to place a guard over it.

As to the Chinese inhabitants they had to inspect them, whether they were suffering from any infectious disease or not. On finding them suffering from such, they provided a special quarter, to which they were sent and where they were treated by the medical officers. As to the houses, which were used as quarters by the soldiers and which had been occupied by Chinese, in the first place, they cleaned the house from corner to corner and disinfected the parts which they considered dangerous, and, also, they thoroughly cleaned and disinfected as much as possible the surface of the soil round the houses as well as that outside of the camping ground. Afterward they removed daily and destroyed all the combustible refuse by burning or burying it. Fecal matter was treated in the same way as is done in other countries.

As to flies, we had considerable trouble with them. At the beginning we tried to kill them in various ways, but they were so numerous that we were practically overwhelmed by them. Soon, however, it was discovered that they lay their eggs in manure as well as in refuse, and since then we tried to burn all the manure and refuse as quickly as possible. We were thus able to diminish the number of flies.

Clothes. Besides washing the clothing as often as opportunities occurred, we had disinfecting apparatus with which the clothing, etc., belonging to each soldier was disinfected or sterilized whenever we thought it necessary to do so. Each apparatus had a capacity of disinfecting for twenty men at a time, and I believe we had to use more than one hundred apparatuses, and I still further believe they were very useful means of preventing any epidemic disease from spreading.

Sending the Troops to the Front. Before the troops were sent out to the field they were made to undergo strict inspection by medical officers to see whether there was suspicion of any form of epidemic disease amongst them. When such was found, all were disinfected before being sent out.

As to transportation of troops from the front back to Japan, all the troops had to be disinfected at quarantine station and were then allowed to land. We are now employing three quarantine stations, the principal of which is that of Ninoshima, where they can disinfect 6000 men in the course of twenty-four hours. As to disinfection, the means employed there are both steam sterilization and formalin fumigation, of which I do not think there is any necessity of description, because they are the same as you have in your own quarantine stations.

All the transport ships were made to undergo thorough cleaning and disinfection each time they came back to the ports, and the space between decks was cleansed and disinfected with steam, etc.

As to the treatment of wounds, our army surgeons were in favor of the conservative surgery and all were treated aseptically as much as possible. In a great many cases, with the first dressings applied, they healed by the end of a week or ten days without the dressings having been changed. Major operations were avoided as much as possible in the front; of course, after evacuation to Japan such have been done according to the nature of the wounds. Various means of treating the wounded in the front were employed according to the nature of the wounds, but, on the whole, aseptic surgery was the principal object. As to the results and terminations of all the cases treated we are not yet in position to inform you because such a large number of troops and medical officers were employed and consequently the reports, which were made in the front, had not yet arrived at the time when I obtained the notes which I have given you here. As one part of the results and terminations of treatment, I give you a short account of the hospital established in Hiroshima.

The hospital was established in April of 1904, and the report covers the period till November 30, 1905, during which time the hospital admitted 203,782 cases, of which 162,885 were transferred to other hospitals. The average number of patients in the hospital was about 5000 and the largest number the hospital had was 10,000 cases at a time. Almost all the serious cases were kept in the hospital because they were unfit to be transferred, yet the result was so good that the ratio of deaths and invaliding is a little above 1 per cent. Almost all the wounds of the soft tissues healed within about ten days, those with injuries to the bones have progressed favorably except those who were wounded at the siege of Port Arthur. Many men who were wounded in the head and chest have recovered from the wounds received. There were many cases of traumatic aneurysm and wounds of nerves requiring operation. The number of operations performed at the hospital amounted to more than 3500.

EMPYEMA IN CHILDREN.[1]

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The etiology, pathology and diagnosis of empyema in children offer a rich field which has been especially investigated by medical writers. It is the more strictly surgical attitude of the subject to which we would call your attention. With this view in mind we have analyzed a series of forty-one cases upon which we have operated, the majority of them in our service at the Philadelphia Children's Hospital, and described in connection therewith, those points concerning the stage at which the disease was encountered, the technique employed, and the results obtained, which seemed to us of the greatest importance from a surgical standpoint. The cases ranged in age from ten months to thirteen years; two were under one year, eight between one and two years, one-half were under four years, and nearly two-thirds under six. There was a slight predominance in the number of female over male children, 58 per cent. of the former to 42 per cent. of the latter. In a large majority of the cases, if not, indeed, in all, there was a history of pneumonia preceding the development of the empyema. This pneumonia was usually of an independent croupous form; in three or four cases it developed as a complication of scarlet fever or measles. In some cases it was still present at the time of operation; in others it preceded it by a number of days, weeks, or even months. When present at the time of operation pneumonia may be a formidable complication, or it may be relighted later in a crippled lung and bring about a fatal termination.

Duration before Operation. Empyema usually follows closely on the heels of pneumonia, and the pleural effusion rapidly becomes converted from a serous into a purulent collection; in some cases, indeed, it is difficult to distinguish between the two at the onset. It follows that when a considerable length of time has elapsed between the onset of the pneumonia and the detection of pus in the chest, one can usually assume that the collection has existed in the pleura for a correspondingly long period, and that the lung is probably bound down by more or less firm adhesions. A large proportion of both hospital and private cases un-

[1] Read before the Surgical Section of the Pennsylvania State Medical Society, September 13, 1906.

fortunately are of this class. Probably many cases perish with a pleural collection unrecognized. Certain it is that many are condemned to a tardy convalescence, to repeated operations, and some to permanent crippling of the lung and secondary deformities of the chest and spine, through failure to recognize the empyema promptly, or to institute the only proper treatment, namely, operation. In two of this series the duration of the condition was so long as to result in "pointing" of the collection in the usual site, namely, the anterior aspect of the chest, near the nipple line, and in two or three other cases not included in this series we have been called upon to do secondary operations in the same class of cases of *empyema necessitatus*, previously drained by our colleagues. Secondary operations in this class of cases are of great frequency, and scarcely less so in those long-standing cases which only differ in the fact that the pus has not burrowed out through a favoring point in the chest wall. In one case the pus discharged into a bronchus before operation, and in another case during operation.

Condition of Patients at time of Operation. The condition of the patients when presented for operation varied considerably. Some were still desperately ill with pneumonia; this is especially prone to be the case with very young children, in whom the mortality is highest. Others presented moderate fever, or normal temperature, were somewhat anemic and showed some loss of flesh, but had recovered from the initial illness and were not yet cachectic and exhausted by long-continued septic absorption; these constituted the favorable class. The neglected cases, usually undiagnosed for a considerable time, were much emaciated, very anemic, sometimes very feeble, and in one fatal case practically moribund at the time of operation. To this class belong the "pointing" cases already mentioned. Considering the duration of these cases, and the condition in which they come to the surgeon, it is surprising how well they sometimes stand operative intervention if they have any recuperative power left, which is especially the case with the older children. In every case, however, the convalescence is tedious, and sometimes incomplete, owing to the lasting adhesions by which the lung is confined.

Nature of the Operations Performed. We believe that aspiration has no place as a curative measure in the treatment of empyema. Much discussion has taken place over the question of the comparative value of intercostal incision and rib resection in the treatment of empyema. In a number of our cases, especially those operated several years ago, we have been content to perform intercostal incision. At the present time, however, the decision of the majority of surgeons is in favor of rib resection, except in a few selected cases. Undoubtedly intercostal incision is sometimes a highly successful operation, but resection has certain unquestioned advantages. It affords much more room for exploration of the pleura, which is of prime importance in encysted collections, and permits of the evacuation of the masses of lymph which are frequently present, and which, if not removed at the time of operation, often cause clogging of the drainage tubes after a few days, or undergo slow decomposition, and furnish a good culture medium for infecting organisms. The close approximation of the ribs interferes with the use of large drainage tubes. Furthermore, the excision of a portion of a rib takes little more time than intercostal incision. Some pediatrists, like Koplik, advise against rib resection in infants under eighteen months, although we have not seen any contraindications to it on these grounds. Where the condition of the patient forbids even a transient or incomplete anesthesia a simple incision should be practised, and only exceptionally in other cases. In very sick children with large collections, preliminary aspiration, twenty-four hours before operation, is deemed advisable.

Technique of Operation. The steps of the operation, as we have practised it, consist in the administration of ether after all preparations for operation and sterilization of the chest wall have been completed. The anesthetic is never pushed, and the operation is carried through with all possible speed. We always make it a rule to aspirate first with the hypodermic needle at the site of our proposed excision and demonstrate the presence of pus. The patient is turned slightly toward the sound side. We prefer an incision with its centre on, or a little posterior, to the postaxillary line, and immediately over the eighth or ninth rib in unencysted collections; where the collection is encysted, the rib corresponding to its lower limit is chosen. The latissimus dorsi muscle will be encountered and partially divided. We have once or twice performed a "muscle-splitting" operation posterior to this point without transverse division of muscular fibres, the latissimus dorsi muscle being split at an angle to the skin wound, and the deeper incision made parallel to the skin incision. This requires a little more time and assistance than the ordinary incision, and has been practised with the intention of lessening postoperative pain. When the rib is exposed its periosteum is divided longitudinally, and a curved periosteal elevator is used to clear the rib in its entire circumference. The periosteum and pleura are pushed downward under the rib with the same instrument, and the rib divided with a pair of bone-cutting forceps, the anterior section being made first, and the divided rib being firmly elevated with sequestrum forceps while the posterior section is made. About an inch of the rib is removed in small children. The periosteum and pleura beneath are then punctured with a knife, and the opening enlarged by the finger or a blunt instrument. If pus is encountered the patient is turned to the affected side to facilitate its escape. The cavity is

explored with the finger, and all masses of lymph cleared out with the aid of forceps. Two large drainage tubes are inserted into the most dependent portion of the cavity, and if there is much oozing of blood a wick of gauze is packed into the cavity. A large and thick dressing is then applied after any bleeding points which have been previously clamped have been ligated. A couple of stitches may be inserted in either end of the wound. The essential steps of the operation can be completed in a few minutes in uncomplicated cases. In encysted collections pus may not be found when the pleura is first opened, and the collection must be sought for by digital exploration and its surrounding adhesions broken through.

Encysted Collections. In a certain number of cases of this series, a small but important minority, the collection was encysted, in one case being interlobar. Sometimes, in spite of preliminary aspiration at the site of operation, the pleura will be opened beyond the limits of the encysted collection, and it will be necessary to break through adhesions before pus is reached. If the collection is posterior to and below the original incision it will then be advisable to make a counter-opening between the ribs at the most dependent portion of the cavity, or to resect a rib at this site. Careful search is always needed before deciding that pus is not present in the pleura. In the case of interlobar empyema operated upon, pus had been detected by deep puncture at the site of rib resection, and when the pleura was opened, and nothing found in the neighborhood but light adhesions, puncture was again made directly through the underlying lung and pus detected. Along this track a director was passed into the collection, the opening dilated, and the collection evacuated through the lower lobe of the lung as one would drain a pulmonary abscess.

After Treatments. No irrigation is used by us during or after operation. We believe irrigation is unnecessary and often dangerous, except in a very few cases. In putrid empyema it may be advisable to use mild irrigation after a few days, but even here efficient drainage will usually render it unnecessary in children. The after-treatment consists in changing the dressings when saturated, usually twice in the first twenty-four hours, and after that at daily intervals, using all antiseptic precautions. The temperature usually falls to normal in three or four days if the drainage is efficient and no complications are present. Secondary elevations of temperature are often indicative of deficient drainage, and the wound should be promptly investigated to exclude any pocketing of pus. Stimulation is often required after operation, strychnine and whiskey being our favorite drugs, and the medical side of these cases needs careful supervision. We must remember, as it has been remarked, that it is a patient and not an empyema that we are treating, and that much depends upon the after-treatment.

Complications. The common complications in the post-operative period which we have encountered were pneumonia, persistent or reawakened, gastroenteritis, which may be violent or even fatal, and a condition resembling marasmus, but really a form of septic poisoning, and usually associated with a pleural collection long overlooked, or treated by palliative measures or insufficient drainage. It is marked by progressive weakness and emaciation. We have not found tuberculosis a common complication in children either in our own experience, or in the reports of other American surgeons.

Tubular drainage is maintained until the discharge has diminished sufficiently to drain by a gauze wick. One tube is first removed, and the other gradually shortened and finally dispensed with. This can sometimes be done in ten days; frequently a longer period is necessary. We are guided entirely by the amount of discharge. Closure of the sinus takes place more rapidly after rib resection than after intercostal incision.

Results. In forty-one cases of all types, primary and secondary, there were eight deaths, a mortality of 19.5 per cent. Excluding six cases of secondary operation in which there was no mortality, the percentage of deaths for acute cases was 22.8 per cent. Most of the fatal cases were in very young children, of two years or younger, the youngest fatal case being eleven months, and the oldest five years of age. The youngest case operated upon was ten months, a nursing babe, which recovered after rib resection. The causes of death were exhaustion, pneumonia, and sepsis. One case was practically moribund at the time of operation and died in a few hours. Another developed a fresh pneumonia and died ten days after operation; and still another died several months later after an attack of pneumonia in a crippled, airless, and fibroid lung. Four were neglected cases of at least several weeks' standing, and in one the pus had ruptured into a bronchus. Four cases were in fair condition at the time of operation, and four were in bad condition, emaciated, exhausted, or in the acute stages of pneumonia or sepsis.

In our experience it seems that very young children with high fever, dyspnœa and rapid pulse are much more unfavorable cases than older children with long-standing collections, but with a certain acquired resistance, who often stand operation remarkably well. There would also seem to be a difference in the virulence of infection in different years, or, speaking broadly, in different epidemics, for the disease sometimes reaches that proportion in hospital cases. This observation has also been made by Scharlau in his work in the Mt. Sinai Hospital. Five of our eight fatal cases were encountered in 1905, while in the present year we have had a series of

ten cases without mortality. In large series of cases of empyema in children the mortality has ranged from 14.4 per cent. (Cotton) to 54 per cent. (Nathan Baginsky's clinic).

Secondary Operations. In five of our own acute cases we were obliged to perform secondary operations. All but one were neglected cases, and in this one the primary collection was encysted, and there was apparently a secondary infection of the uninvolved portion of the pleural cavity. All these were primary rib resections, except one in which Dr. Le Conte had made a preliminary incision on account of the desperate condition of the patient. Four recovered, and one died later of pneumonia, probably septic, in the crippled lung. Of six secondary operations on cases primarily operated by other surgeons, all recovered from operation. One child has been operated several times since in the Children's Hospital, and is a most pronounced type of high-grade primary and secondary deformity of the chest and spine. Two are known to have been cured, and the remainder were discharged from the hospital before complete healing, but were improving and were probably cured.

Resection of one or more ribs after the manner of Estlander has been the type of operation performed in these secondary cases. We have had no experience with the more severe operations of Schede or Fowler-Delorme in children. The latter operation, lung decortication, has yielded good results in children in the hands of Dowd and others.

SOME OBSERVATIONS UPON THE STRUCTURE OF THE SPIROCHETA PALLIDA (SCHAUDINN).

By Herbert Fox, M.D.,
Volunteer Associate, William Pepper Laboratory of Clinical Medicine.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

The object of this communication is to record some observations on the morphology of the spiral body found by Schaudinn and Hoffmann in preparations from syphilitic eruptions. The material at hand consisted of smears from six chancres, three mucous patches, three maculopapules, three secondary variolous syphilides, one venereal wart, sections of one of the mucous patches and of the venereal warts. A comparative study of the secondary eruptions with a chancre (author's case) was made possible by the gift of an excised mucous patch and venereal wart from Dr. Rosenberger, whom I wish to thank at this point.

Pressure preparations were made on slides exclusively, avoiding as much as possible any rubbing which might alter the position of the organisms, or distort them. Tissues were preserved in 4 per cent. formalin.

The staining methods used were: Giemsa (ten minutes' fixation in absolute alcohol and one to two hours' staining), Goldhorn's borax methylene blue, Wright's blood stain, filtered saturated aqueous solution of gentian violet, iron-hematoxylin, and the silver precipitation method modelled after Levaditi but somewhat modified for use with slide smears. The first two are very good for diagnostic purposes, especially the second when differentiated with Lugol's solution; but for study of the form, shape, and especially the ends of the spirals the last three were found to be the best. The silver precipitation method is as follows: Fixation in 10 per cent. formalin thirty minutes, 95 per cent. alcohol thirty minutes, 1.5 per cent. solution silver nitrate twenty-four hours, pyrogallol solution (pyrogallol 4 per cent., formol 5 per cent.) four hours, wash in running water, clear with alcohol and bergamot oil, and mount. This may or may not be stained. The field is quite dirty but it has been impossible to obviate this so far. The organisms may be seen quite clearly when found free from precipitate. This method is only useful for study and has no value in diagnosis.

It is hardly necessary to go into the percentage of findings in my material further than to say that the results are in accord with those of others. The variations of size will be considered later, but the evidences of flexibility indicated by the position of the spirals in pressure preparations, and the irregularities of staining have been reported many times. These appearances seem to be more characteristic of the Sp. refringens than of the Sp. pallida.

Herxheimer and Loeser have reported the finding of spindle-like bundles and rosette arrangements of these spirochetæ, simulating segmenting trypanosomata. Such an arrangement has never been seen in any of my preparations. In smears the organisms are usually single; two or three may be seen more or less closely intertwined at some point of the length; two individuals are sometimes encountered lying parallel with their coils closely interlocking, giving the appearance of longitudinal division. In tissue they are most frequently single, and when present in large numbers lie more or less parallel to the tissue structure; masses of spirochetæ are without definite arrangement. The long axis of the body of the organism is commonly straight when seen in tissue, but in slide stains, no matter how carefully made, the spirocheta is most often bent, even to the extent

of forming a circle, which fact is not difficult to explain if we imagine one end drying before the other. In all probability these shapes are largely artificial.

Examination with high apochromatics and compensation oculars has not developed any undulating membrane or contractile pore either in the moist or stained (iron-hematoxylin) state.

Evidences of what might be considered longitudinal division have been observed four times in all the preparations studied, while undoubted transverse division has been seen many more times. The transverse division is characterized by the appearance of a palely staining area at or near the middle of the spiral, with subsequent thinning and separation of the extremities into two new individuals. On one occasion transverse division into three elements was noted. It seems that the newly formed or newly forming spirals have more curves in relation to their length than the individuals apparently older.

On the other hand the indications of longitudinal division are not clear, the best example being shown in the drawing(*B*). Here the free end is fine and tapering, while the end near the larger spiral has the same diameter as that body at their point of contact. They must have be enclosely associated, since no power of the microscope at my command could dissolve them at their point of junction. This was seen in a stain from a chancre.

Many times intertwined spirals were met with, but in almost every instance both ends of each body could be discovered by diligent search.

A word will be added here in reference to this matter of division which will have a relation to what will follow. Only the large typical forms of the "pallida" show this simulation of longitudinal division, the shorter type always segmenting transversely.

When comparing the preparations made from chancres and from secondaries, I was struck with the fact that the forms of the "pallida" met with in the initial sore are more typical and regular in their shape and size than those met in the later manifestations. They are spirals of an average length of 11.14 microns with an average number of windings of 10.2; their curves form the large arc of a small circle. By careful observation with high powers of magnification in all preparations, even the azur stains, one end may be seen to be thicker than the other. The thinner end fades away into a fine filament called by Schaudinn the flagellum, but which appears to be more exactly a continuation of the body of the spirillum, a view expressed by Norris, Pappenheimer, and Flournoy in regard to Sp. Obermeieri. With the silver method this extremity is blunt and has not the appearance of a whip. On one spiral, by this method, a straight tail was seen to come off this finer end and appears to be a flagellum (Fig. 1). The thicker end is not only wider but takes the stain more deeply, especially when the silver or gentian-violet methods are used. A filamentous extension of this end was never observed, nor could any definite structure be made out. Beyond this blunter end no prolongation can be discovered and there seems to be no spot at or near the *fine* end of the body which is comparable to the clubbing, in other words no thickening from which the terminal filament or flagellum comes off. Nor could

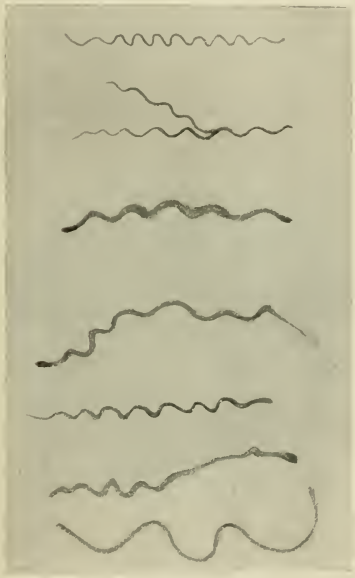

FIG. 1.—*A*, typical Sp. pallida (gentian violet); *B*, evidence of longitudinal division (gentian violet); *C*, shorter form with regular coils and more equal ends seen in secondaries (silver preparation); *D* and *F*, irregular large type seen in secondaries (silver preparation); *E*, typical Sp. pallida showing how the relations between the ends are maintained in silver preparation; *G*, Sp. refringens (silver preparation).

this terminal filament be traced back into the body of the spiral as a differentiated line. Fig. 1 *A* (gentian violet) and *E* (silver preparation) in the drawing show the appearance of a typical "pallida" from a chancre; and in both, the clubbed and fine ends are easily made out. I was unfortunate in photographing the large form and am obliged to substitute a drawing. Fig. 1 *B* represents longitudinal division, if it be division, proceeding from the fine end of this form. Schaudinn supposes that when two flagellæ are seen, divi-

sion is beginning, a reasonable assumption if this spiral be a protozoon. If it be a protozoon one might expect to find a basal body at the root of the flagellum, but such a spot cannot be made out at the fine end of the spiral. The blunt extremity of the spirocheta may contain such a body but this study can offer no elucidation upon this point since sufficiently clear evidences of longitudinal division were observed so seldom. The picture in the drawing was encountered only once. The blunt end *may* be the blepharoplast itself, with the body unstained, the spiral we see being the undulatory membrane or the two latter combined.

In the secondaries, besides the form described above, one meets such types as shown in Fig. 1 *D* and *F*, also in Fig. 2. These represent some of the atypical spirochetæ which appear to be the same as the ones described above. They

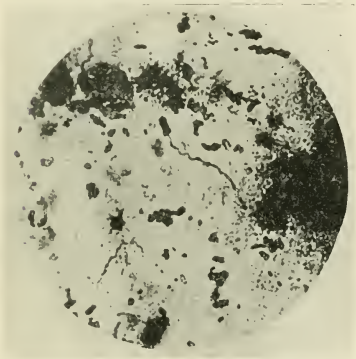

Fig. 2.—Spirocheta pallida, large atypical, by circa 2000 (silver).

have been observed before and explained as artificial productions. Their curves assume for the most part the usual large arc of a small circle, but portions of the length may be found without any curvature. They are not infrequently seen with one or the other end nearly straight, as in the pictures. In these forms the thick extremity is commonly well-marked. One of these is seen in about every ten individuals.

Besides these a shorter slightly thicker form (especially in the silver preparations) may be seen in the secondaries; they are depicted in Fig. 1 *C*, also Fig. 3. This form is usually quite regular and both ends have nearly the same diameter, although one end may sometimes slightly exceed the other; in the photograph one extremity is a trifle clubbed.

It has been suggested that this clubbing is a coil of the terminal filament, but upon search through simple stains no such position of the fine end could be found. With the silver method both ends stain with the same intensity and with gentian violet both ends take the stain badly. The average length of this small form is 10.1 microns and the average number of windings is eight. These are met with

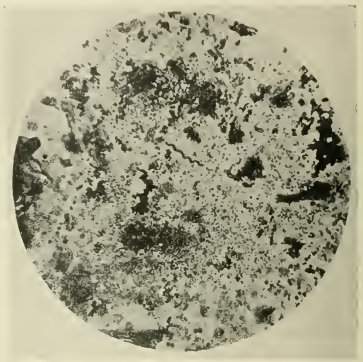

Fig. 3.—Spirocheta pallida, small atypical, by circa 1800 (silver).

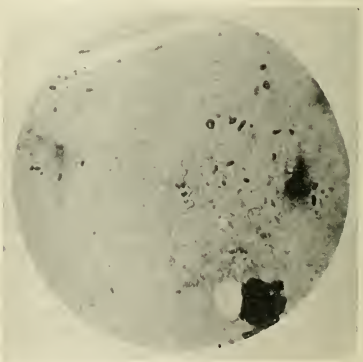

Fig. 4.—Spirocheta refrigens, by circa 1800 (gentian violet).

about once among twenty spirals. They may be differentiated from the Sp. refringens by the fineness and apparent flexibility of the latter in the silver mounts, by the facts that the coils of this spiral form a small arc of a large circle and the ends are of the same thickness and take the stain with equal intensity. The average length of the Sp. refringens

is 12 microns and the number of curves averages six (Fig. 4).

The bulbous ends were not found on spirals in smears from Vincent's angina, the normal mouth, carious teeth and an ulcerated surface.

Although these forms were observed in the material at hand it should be emphasized that I lay no importance upon them as characters of sex, age, stage of development, involution, correspondence to the stage of the disease or nature of the lesions. They may assist in settling the nature of the spiral, however. Since none of the essentials of the protozoa have been found, the proper classification remains an open question. Zetnow has lately discovered that the flagella of the Sp. pallida, unlike those of the bacteria, will stain with methylene blue. The term "Sp. pallida" has been used in this paper, since we have no exact nomenclature at present. Realizing the differences from the bacteria and from the protozoa (flagellata) Schaudinn has suggested the name "Treponema." We will hope for further information to establish the identity of the Sp. pallida.

I wish to acknowledge my thanks to Dr. Lavenson for assistance in preparing the photomicrographs.

BOOK REVIEWS.

THE VERMIFORM APPENDIX AND ITS DISEASES. By HOWARD A. KELLY, A.B., M.D., Professor of Gynecology in the Johns Hopkins University, and E. HURDON, M.D., Assistant in Gynecology in the Johns Hopkins University, Baltimore. With 399 original illustrations, some in colors, and 3 lithographic plates. Philadelphia and London: W. B. Saunders & Co., 1905.

There can be nothing but praise written of this magnificent volume of 800 pages upon the diseases of the vermiform appendix. The illustrations alone have a distinct teaching value without any text and do not suffer by comparison with any other work on medicine or surgery.

The history of the development of the modern teaching of the disease is skilfully traced, and shows how in appendicitis as in other affections a better pathology and therapeusis were advanced by many scattered observers, but delayed in general acceptance because of the views of "eminent authorities." Among the early pioneers, Mélier (1827), Volz (1846), and George Lewis, of New York (1856), are referred to as supporting an international tripos. As is usual in the various books written upon appendicitis, Reginald Fitz, of Boston, receives great credit for his epoch-making paper published in 1886.

The section upon the anatomy of the appendix is most complete, especially the chapter upon the lymphatics, which, while of course indebted to Lockwood, is the most complete exposition the reviewer has ever read. It is gratifying to note that the existence of an anastomosing arterial branch from the ovarian is not credited.

In the section upon Physiology a small research by Dr. Hurdon is included, recording the experimental observation of peristaltic movements of the appendix. The chapters upon the Pathology of the Appendix are very interesting and abundantly illustrated. Some exception might be taken to the classification and to suggest that catarrhal, diffuse, ulcerative, and gangrenous types are sufficient for the acute process. The catarrhal form must be rarely observed in an appendix removed from a patient presenting symptoms of *real appendicitis*, and it is probable that most of the organs classed as acute catarrhal are in reality chronic types.

Kelly rightfully emphasizes the importance of peritoneal complications, because after all it is the peritonitis that causes the mortality and the treatment of which is responsible for much of the diversity of opinion among abdominal surgeons.

The symptomatology and diagnosis of appendicitis are discussed in the main satisfactorily, the only criticism that suggests itself being the continual recitation of a few points in reported cases which increases the size of the chapters, but does not seem to add any clearness to the description of the clinical course of the disease. The importance of tenderness as a symptom is emphasized, and it would be well for every practitioner to remember the statement that tenderness "usually persists after spontaneous pain has ceased, and is present as long as an active inflammatory reaction is going on."

The chapters upon Appendicitis in Typhoid Fever and Appendicitis in the Child are excellent, especial note being made in the latter chapter of the danger of mistaking pneumonia and pleurisy for appendicitis.

The indications for operation are discussed in a sane and careful manner and represent the opinions of the best men of this period. Kelly considers that "the ideal time for operation in acute appendicitis is within the first few hours;" in cases seen during an intermediate period the decision of immediate operation depends upon the exigencies of the individual case and the personal experience of the surgeon; in desperate cases, "the only contraindication to operation is the certainty of approaching death."

In discussing the medical treatment Kelly condemns the use of free purgation during the early stage of an acute attack, contenting himself with small oil enemas.

The operative technique is freely considered, many illustrations excellently showing the various procedures. The latter chapters in the volume discuss the complications and sequelæ, neoplasms, specific infections, and the medico-legal aspect of appendicitis. In considering the treatment of fistula, mention is made of the use of rectal enemas, but reference to the distinctly deleterious action of purgatives by mouth is omitted.

The authors can be commended for producing the most exhaustive study of appendicitis that has yet been written, and the publishers for the general excellence of the book.

G. P. M.

Text-book of Medical Jurisprudence and Toxicology. By John J. Reese, M.D. Seventh edition revised by Henry Leffmann, A.M., M.D. Philadelphia: P. Blakiston's Son & Co., 1906.

The seventh edition of a text-book needs little praise and less condemnation from the reviewer. Leffmann's revision of the recent and concise presentation of the subject of medical jurisprudence has kept it well abreast of the new developments in this field. In this edition new matter has been added in connection with the legal aspects of the use of the Roentgen ray. Some new material has been added to the subject of toxicology, more especially in the subjects of chronic poisoning by acetanilid, potassium chlorate, carbon monoxid and the acute poisoning by formaldehyde, resorcinol, worm seed and boric acid. The serum test for blood is not treated as fully in this edition as its importance demands. The possible exceptions to its accuracy as a test are not mentioned.

The book can be recommended to students as a comprehensive and fairly full presentation of this most important subject. D. J. M.

Nursing, its Principles and Practice for Hospital and Private Use. By Isabelle Hampton Robb, Graduate of the New York Training School for Nurses attached to the Bellevue Hospital; Late Superintendent of Nurses and Principal of the Training School for Nurses, Johns Hopkins Hospital, Baltimore, Md.; Late Superintendent of Nurses, Illinois Training School for Nurses, Chicago, Ill.; Member of the Board of Lady Managers, Lakeside Hospital, Cleveland, Ohio; Hon. Member of the Matrons Council, London, England. Third edition, revised and enlarged. Illustrated. Published by E. C. Koeckert, Cleveland, Ohio, 1906.

In this third edition of 534 pages there has been a thorough revision of the previous editions with the addition of about 50 pages. The first chapter has been entirely changed. Instead of the two years' course previously recommended, an outline is given for one lasting three years. This chapter well emphasizes the value of didactic teaching in preparation for and along with the actual work in the wards. The course as outlined is well arranged, thorough, and should be practical, though in an active hospital the didactic teaching is often sacrificed for the work in the wards. The subject of nursing is treated in all its details. The construction and arrangement of public and private wards, their proper care and hygiene, methods of treatment, medicinal and mechanical, and the keeping of records are well discussed as introductory to nursing in the general medical diseases to which the last 250 pages of the book are devoted. A short description of each disease is given, quite intelligible to the average nurse, and yet quite necessary for the proper performance of the work she has to do. The chapter on surgical technique with directions as to asepsis and antisepsis and the preparation of instruments, ligatures, and suture materials for operations should prove instructive to those in charge of operations in hospitals or private houses. The subjects of pregnancy, labor and the newborn are well discussed and valuable information and instruction given. The book is thorough and well written, leaving little to be desired in an up-to-date treatise on nursing in all its phases. F. H. K.

Yellow Fever Prophylaxis in New Orleans in 1905. By Robert Boyce, M.B., F.R.S., Liverpool School of Tropical Medicine. Memoir XIX, April 1906. Published by Williams Norgate, London.

This memoir traces briefly the development of our knowledge of the mode of transmission of yellow fever by Stegomyia fasciata, and gives in detail the measures instituted in New Orleans in 1905 to arrest the progress and eradicate the disease.

The extension of the disease over a considerable area before its presence was realized; the fact that rain-water collected and stored in open cisterns constituted the general water-supply; and especially the preference of the stegomyia for water of this character for breeding places, made the work of exterminating the mosquitoes one of gigantic proportions.

The measures employed, which were the outcome of the brilliant investigations of the U. S. Army Commission working in Cuba in 1899, and to which the arrest of the disease in New Orleans must be attributed, were: (1) Careful screening of all persons suffering with fever so as to prevent the infection of mosquitoes by such individuals; (2) screening of all water cisterns and placing oil on the water in cisterns, cesspools, stagnant ponds, etc., to prevent the hatching of additional mosquitoes; (3) screening all houses, and the burning of sulphur to destroy the adult mosquitoes in all buildings throughout the city. D. H. B.

A Treatise on Diagnostic Methods of Examination. By Prof. Dr. Hermann Sahli, Director of the Medical Clinic, University of Bern. Edited, with additions, by Francis P. Kinnicutt, M.D., Professor of Clinical Medicine at Columbia University (College of Physicians and Surgeons), New York; Physician to the Presbyterian Hospital; and Nathaniel Bowditch Potter, M.D., Visiting Physician to the City Hospital and to the French Hospital, New York. Authorized translation from the fourth revised and enlarged German edition. Philadelphia and London: W. B. Saunders & Co., 1905.

A translation of such an excellent work is always welcome to the large number of readers unable to avail themselves of the original, but when carefully edited with additions it is gladly received by all.

Sahli's "Klinischen Untersuchungs Methoden" has long been in some respects the standard for works of this kind, its thoroughness, freedom from insufficiently tested methods, and well-executed endeavor to be comprehensive and easily

understood have gained for it this reputation. The additions Kinnicutt and Potter have inserted are concise and apt, and do not seriously increase the already rather large size of the book; the number of excellent illustrations they have added perhaps might be criticised on this score, especially the *x*-ray photographs. The advisability of cutting this book into two volumes has probably been given thought and there must be good and sufficient reasons for its present form, that of one volume of slightly over a thousand pages. Combining as it does physical examination with laboratory examination a logical reason for separation would not be hard to find.

The book is one that all should have and read carefully, especially the first 300 or more pages dealing with physical examination. That part of the book describing laboratory technique will prove useful to all engaged in this line of investigation, the method of explaining the various tests is clear and they can be readily followed out by anyone, which is what Sahli states has been his desire. Unlike some writers on this subject, the author has introduced a large element of personality and thereby increased the interest and value of the book.

There is no inequality of merit throughout the work, one chapter being on a par with all others. W. P.

A Treatise on Surgery. By George Ryerson Fowler, M.D., Brooklyn, New York City; Examiner in Surgery, Board of Medical Examiners of the Regents of the University of the State of New York; Emeritus Professor of Surgery in the New York Polyclinic; Surgeon to the Methodist Episcopal Hospital; Surgeon-in-Chief to the Brooklyn Hospital; Surgeon to the German Hospital. Containing 888 text illustrations and four colored plates, all original. Vols. I and II. Philadelphia and London: W. B. Saunders & Co., 1906.

In this treatise on surgery by George Ryerson Fowler the medical profession and students will welcome a valuable addition to their library. The author has successfully collected the innovations advanced in surgery during recent years and so combined them with his own experience and practices as to make the work an exceedingly interesting and useful one. The grouping of various topics, though somewhat unusual, seems surgically clear and logical. It leads the reader by easy stages rationally connected through realms of theory and technique to regional and operative surgery. The chapter devoted to laboratory methods and the importance of results obtained from them is especially valuable in the light of the constantly increasing dependence of clinicians on hematology, urinology, pathology and other similar subjects. Surgical bacteriology likewise receives well-merited attention and the symptoms, diagnosis, and treatment of the various wound fevers are clearly and concisely enumerated. After a thorough discussion of anesthesia and operative technique in general the author approaches the subject of regional surgery. Here he adopts the anatomical method, reviewing all pathological conditions to which a part is subject. The diagnosis and treatment are always clearly indicated, and when operative proceedings are devised the steps of the operation, its accompanying dangers, and after-treatment are so pictured as to leave a lucid and lasting impression upon the reader's mind.

A word of praise is due the 900 original illustrations. Wherever possible the author has photographically shown the succeeding steps of operations, anatomical landmarks being demonstrated with a clarity that would grace purely anatomical work. In conclusion, we feel highly gratified in recommending Fowler's *Treatise on Surgery* to the profession. Its methods are such as to render it peculiarly well adapted to purposes of reference for student and practitioner alike, and it therefore well merits a place upon the shelves of every complete library. J. J. A. VanK.

Nursing in the Acute Infectious Fevers. By George P. Paul, M.D., Assistant Visiting Physician and Adjunct Radiographer to the Samaritan Hospital at Troy, N. Y. Illustrated. Philadelphia and London: W. B. Saunders & Co., 1906.

In this little book of 200 pages, Dr. Paul gives us a short discussion of the acute infectious diseases with brief and pointed directions as to their immediate care and management. The book should appeal especially to the graduate nurse in her work in private houses, though it is not without interest and help to the young practitioner who is apt to overlook some of the many details in the handling of acute diseases. The book is divided into three parts. The first deals with general subjects and acts as an introduction for the second part, in which the acute diseases are discussed individually. The third part is taken up with a few special subjects for the better understanding of the second part The discussions and directions are brief and to the point, and presuppose a fairly good acquaintance with medical terms and methods. Although treating of the acute infectious diseases, the methods and directions given can be well applied to any form of nursing. F. H. K.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

COXA VALGA OR COLLUM VALGUM.

By James K. Young, M.D.,

Associate in Orthopedic Surgery, University of Pennsylvania; Professor of Orthopedic Surgery, Philadelphia Polyclinic; Clinical Professor of Orthopedic Surgery, Woman's Medical College of Pennsylvania.

Since Müller first called attention to coxa vara it has been carefully studied in all its various phases, but the opposite condition, coxa valga, has received but little notice, and a few authors only have written upon the subject.

Coxa vara is considered as a serious clinical disease, but coxa valga is simply described as an anatomical or pathological change in the direction of the neck of the femur.

The modern text-books do not even mention the subject, describe it superficially, or include it as a form of coxa vara, so that the medical profession in general are not familiar with the symptoms, and in some instances are not even aware of the existence of this deformity.

Under these circumstances it seems not unsuitable to present the following cases which have come under my personal observation.[1]

COXA VALGA FROM TRAUMATISM, PROBABLY FRACTURE OF NECK OF FEMUR.

Case I.—"D. D.," an Italian boy aged eight years, with a family history free from any hereditary taint, was brought to me for examination in January, 1906, by Dr. M. A. Roberts. About five years ago the child fell, after which his mother noticed that he walked "crooked." The deformity has b en increasing of late. When he falls down he has difficulty in getting up.

Examination of patient revealed the following condition:

Patient stands on left leg with right knee thrown forward and inward, the lumbar spine curved, with the convexity to the right, and with left shoulder depressed. In walking he limps on the right leg. In standing the creases of the buttocks are inclined to the left, and the abdomen is pendulous and prominent. In the lying position there is slight lordosis and the pelvis is tilted upward on the right side. The right leg is apparently longer than the left, although the bony measurements are the same. In the right hip flexion is abnormal, the thigh is carried outward in abduction during flexion, and adduction is then limited. In the left hip all movements are normal. The right limb is adducted upon the pelvis. Flexion of both knees shows the femur of the right limb to be a little longer than that of the left, and the lordosis is not entirely lost until both thighs are flexed upon the abdomen. The spine is flexible in every direction, and there is no osteitis present.

Skiagraph shows angle of neck of femur on right side to be decreased to about 142°, while on the left it is 132°.

On the right side the angle of depression is 142°.

On the right side the angle of elevation is 48°.

On the left side the angle of depression is 132°.

On the left side the angle of elevation is 36°.

I divided the adductors from their pelvic attachment, encased the leg in plaster, and abducted the limb for two weeks.

Case II.—*Coxa Valga from Forceps Delivery.* "P. R.," a girl aged four years, with a family history of cancer and tuberculosis. Mother primipara, rachitic and delicate; child born by breech presentation after long and difficult labor. Forceps were applied to breech until traction could be made on feet. No traction was made on head. Child was weak in infancy. Had whooping-cough when four months old, which lasted until ten months old. Child never crept nor attempted to hitch herself along the floor; during the past two weeks (now four years old) has attempted to stand, but not alone.

Present Condition. Child small and delicate looking. Poor muscular development. Teeth fair. Mental development normal. Does not sit up well and prefers to lie down. Mother has noticed that child is left-handed, and right arm seems slightly spastic, and has slight wrist-drop; grasp weaker. Both lower limbs stiff; feet held in equinus position; patellar reflex delayed and exaggerated; limbs poorly developed. Stands when supported in position of equinus, with knee flexed and right foot advanced. Length of spines—to malleolus—right, 16½ inches; left, 16¼ inches. Bryant's triangle destroyed on right side. Trochanter posterior to and 1 cm. below Nélaton's line. Limbs held in adducted position; can be only slightly separated. Abduction very limited, with spasm of adductors noticeable. Internal rotation possible on left side, but very slightly so on right. Flexion of thigh on pelvis difficult. Outline of thigh and hips abnormal on both sides.

Skiagraph shows coxa valga on both sides, more marked on right, and also shows marked backward displacement of trochanter on right.

[1] I am indebted to Dr. Stella Hager, Clinical Assistant, Philadelphia Polyclinic, for valuable assistance in the preparation of this article.

FIG. 1.—Case II. Coxa valga from forceps delivery. Front view.

FIG. 2.—Case II. Coxa valga from forceps delivery. Back view.

FIG. 3.—Case II. X-ray photo. Coxa valga from forceps delivery, showing extreme angle of depression.

On the right side the angle of depression is 174°.
On the right side the angle of elevation is 86°.
On the left side the angle of depression is 164°.
On the left side the angle of elevation is 79°.

Case III.—*Coxa Valga from Separation of Epiphysi.* "A. R.," a Russian boy four years old, with a negative family history was admitted to the Polyclinic Hospital February 6, 1906. Two years before admission while robust and in perfect health, the child fell. Complained of severe pain in righ hip, which was worse at night, but continued to walk with decided limp for one week.

Examination revealed the following:

The right leg is shortened one inch. There is fulness about the right trochanter. There is no abduction. An *x*-ray photograph showed a separation of the head and epiphysis of the femur on the right side. Bed traction of five pounds was applied, the limb being in an abducted position in order to avoid coxa vara. He was discharged cured four weeks from the time of injury.

On May 6 he was re-admitted on account of stiffness in the right leg which is more prominent in the morning on rising. He limped slightly on walking, and this is more noticeable when tired. The pain is not referred to the knee. He cannot lie on the right side, but sleeps well. His general condition remained good. Examination at this time showed the clinical symptoms of coxa valga, which was confirmed by the *x*-ray.

On the right side the angle of depression is 144°.
On the right side the angle of elevation is 58°.
On the left side the angle of depression is 133°.
On the left side the angle of elevation is 33°.

Case IV.—*Coxa Valga from Knee-joint Disease.* "W. B.," a boy two and one-half years old, of German extraction, was referred to me by Dr. W. D. McConaghy on March 30, 1904. There was no family history of rickets or tuberculosis, and he was well and strong until February, 1903, when he sustained a slight traumatism of the left knee and hip. Extension was applied for three months, followed by a cast to the knee-joint. While wearing this cast (October, 1903) an abscess formed and a superficial sequestrum was removed from the outer condyle of the femur, which contained tubercle bacilli. Upon the healing of the sinus (January 10, 1904) he was allowed to walk. The biceps tendon began to contract at this time, and it was for this he sought advice. Examination showed an ankylosis of the left knee-joint from tuberculous arthritis, complicated by the clinical symptoms of coxa valga. The affected limb was one-half inch longer. This diagnosis was confirmed by the *x*-rays.

On the right side the angle of depression is 130°.
On the right side the angle of elevation is 42°.
On the left side the angle of depression is 160°.
On the left side the angle of elevation is 68°.

I divided the biceps tendon, and equalized the limbs by a sole on the sound side. The leg became one-quarter inch shorter.

Case V.—*Coxa Valga from Rickets.* "L. N.," a Russian boy aged four years, was admitted to the Polyclinic Hospital April 13, 1906.

Family History. Family history was negative as regards any hereditary taint bearing upon the present condition.

Present History. Mother noticed peculiarity in child's walk about two months ago, child becoming rather shuffling in his walk, the right leg apparently being affected. Condition has been getting worse.

Fig. 4.—Case V. Coxa valga of right leg from rickets.

Examination. Examination upon admission showed the following conditions: Patient is a well-developed child; well-nourished. Was born after normal labor, no instruments being required. Was breast-fed for first two years of life. Epiphyses are slightly enlarged and abdomen prominent, but no other evidence of rickets. No history of injury. Patient stands resting the weight on the left leg with the right foot slightly advanced and the knee flexed. He walks with a decided limp on the right side. In the prone position the right foot is slightly averted, the knee slightly bent, and the thigh slightly abducted. Forced flexion is limited. Abduction is extreme and adduction slightly limited. There is no contraction of the tendons about the knee or hip. The right leg is apparently longer than the left. The left hip,

as well as the pelvis and vertebræ, appears to be normal. Patient does not complain of pain and there is no evidence of pain during the examination. Skiagraph shows the neck of the femur in the right leg to be in a position of coxa valga.

On the right side the angle of depression is 150°.

On the right side the angle of elevation is 63°.

On the left side the angle of depression is 140°.

On the left side the angle of elevation is 35°.

Definition. Coxa valga may be described as a deformity of the hip-joint due to an increase in the angle of depression characterized by marked external rotation and increased abduction with limitation of adduction.

Relative Frequency. In order to determine the normal angle of the neck of the femur as well as the relative frequency of coxa valga and coxa vara, I[1] have taken the measurements of a large number of specimens in the Museum of the College of Physicians and the Wistar Museum in Philadelphia. These were mostly adult specimens of all nationalities and both sexes. Measurements were made of the angle of depression and the angle of declination. The greatest difficulty was experienced in taking the angle of declination, and in some instances it was necessary to have sections of the bones made to determine them accurately. Any angle of depression between 110° and 135° was considered normal, and any angle below 110° was considered as coxa vara, and above 140°, coxa valga. The lengths of the femur were considered but are not recorded here. The number of femurs examined at the College of Physicians was 206, and at the Wistar Museum 615, making a total number of 821. Of these there were 8 cases of coxa valga, or 0.97 per cent.; 52 coxa vara, or 6.33 per cent., and the remainder were normal; over 75 per cent. of these having an angle of 130°.[1] Of the specimens of coxa valga examined, 1 was due to tuberculous osteitis; 4 to arthritis with exostosis; 1 to rickets; 1 to hydrocephalus; and in the others the cause could not be determined from the records. The angle varies from 138° to 150°.

The specimen of coxa valga from hydrocephalus is exactly similar to one reported by Humphreys in the Cambridge Museum. In his specimen the angle of each neck was 148°; in mine, 152°. No example of coxa valga from amputation of the femur in early life like those observed by Turner and Humphrey were observed. All of the eight specimens of coxa valga examined were unilateral except the one due to hydrocephalus.

Fig. 5.—Case V. X-ray photo. Coxa valga from rickets.

No. 1. 1174–34–4. Angle of 145°. Arthritis and deformity of head.

[1] With the assistance of Dr. John Read, late Resident Physician, Philadelphia Polyclinic Hospital.

[1] Of eleven fetal skeletons examined at the College of Physicians the development was not sufficient to allow of any exact measurements. The head and neck in these specimens were ligamentous and usually in the axis of the shaft. The measurements of the angles of the infant skeletons showed the usual high angles recorded by other writers.

Infants: Wistar Museum.

4201.	Three years.	Angle of inclination 135°.
4205.	One year.	Angle of inclination 145°.
4202.	Eleven months.	Angle of inclination 145°.
4203.	One year, forty-four days.	Angle of inclination 150°.
4201.	Two weeks.	Angle of inclination 145°.

No. 2. 1175–34–4. Angle of 142°. Upper one-third of left femur, caries of head and neck. Head and upper part of neck missing. Adjacent surfaces of bone are rough and show more or less periosteal deposit. In the remains of the neck there is a cavity 1.5 cm. deep but not showing any sinus. Vertical section shows a healthy shaft and healthy spongy tissue of the trochanter major.

No. 3. 1168–35–4. Angle of 142°. Arthritis and exostosis of head. There is no malformation except at the junction of the head and neck, which is marked by a thick and prominent overhanging ridge of bone. At the inner side of the head this ridge is prolonged to the pit for ligamentum teres.

Fig. 6.—Coxa valga from hydrocephalus. Angle of 152°.

No. 4. 1171–35–4. Angle of 150°. Arthritis and deformity of head. Exostosis and eburnation.

No. 5. 1229–34–6. Angle of 150°. Anterior bowing of shaft of bone. Axis taken from upper shaft. Rickets, adult bone, but only 31 cm. in length. Posterior wall thick, anterior wall thin.

No. 6. 430–17. Angle of 150°. Skeleton of negro child, aged six years. Hydrocephalus, bilateral coxa valga. Circumference of head 70.5 cm. (27.75 in.). The long bones are thin and delicate, and the entire skeleton light in weight.

No. 7. 2069. Angle of 145°.

No. 8. 10,300. Angle of 145°.

In order to make the examination of the specimens of value every femur in the collection was accurately measured. In this manner it was found that there were 52 specimens of coxa vara. Among the 821 femurs, 21 of these were found among the 206 specimens in the collection of the College of Physicians, which contains mostly pathological material, and 31 were in the Anatomical Institute. The angles varied from 40° to 109°. There were a large number of specimens of impacted fracture of the neck of the femur with angles below normal but these were omitted.

Etiology. The normal angle of the neck of the femur is formed by the opposition of two forces: muscular action and superincumbent weight, these forces being usually sufficient to counterbalance each other and produce a normal angle. If anything should interfere with this harmonious antagonism and the weight pressure should be removed, or the muscular force should overbalance the weight pressure—the open angle will remain or there will be a reversion to the obtuse angle of fœtal life.

Since coxa valga is dependent upon different pathological conditions a classification founded upon its etiology will be found most satisfactory. Thus coxa valga may be: I. Congenital, (1) not associated with congenital deformities of other parts, (2) associated with congenital luxation of the hip. II. Acquired, due to (1) static causes, (2) an incomplete fracture, separation, or displacement of the epiphysis, (3) rickets, (4) osteomalacia, (5) osteomyelitis, (6) exostoses, (7) tuberculosis.

Congenital. 1. Not associated with congenital deformities of other parts. The existence of coxa valga as a primary congenital affection is established by the publication of a congenital bilateral case by David, in which neither rickets nor injury could be demonstrated as antecedent to the deformity. No other congenital cases have yet been reported, but if the attention of surgeons be directed to this deformity the congenital variety will probably be more commonly observed.

2. Associated with congenital luxation of the hip. It may be questioned, as it was in coxa vara, whether the deformity of the neck associated with luxation of the hip should be considered as coxa valga since the head is out of the acetabulum. The measurement of the angle of elevation proves that these cases should be placed in the category whether associated with luxation or not, and when reduction has been accomplished the clinical symptoms will be identical with luxation. Schulthess and Luning give an *x*-ray illustration of this kind, and Schede has two excellent examples of bilateral luxation showing the increased angle.

Acquired. 1. *Static.* By far the greater number of illustrations, clinical or pathological, have been the result of static conditions. In some instances, as in scoliosis, the unequal distribution of the body weight produces a

compensatory coxa valga, and contraction of certain muscles, as the adductors, is sufficient to overcome the pressure force and the open angle results. The same unequal distribution of weight produces coxa valga in luxation of the other hip, or in genu valgum of the opposite side, as in Gangolphe's cases. If during adolescence, and more rarely later in life, the superincumbent weight is sufficient—as in hydrocephalus—or is removed by paralysis, amputation, or the patient is bedridden, or weight is removed from the part by reason of joint disease, the angle present during adolescence remains or is increased. Under these circumstances, in addition to the absence of the beneficial effect of superincumbent weight, the dangling and hanging of the paralyzed extremity, or the amputated stump, produces a continuous extending influence upon the neck of the femur, increasing the angle of depression. Under this head would fall the amputation specimens of Humphrey and the two cases of amputated stumps of Lauenstein. Another and rarer static cause of coxa valga is sciatica and neuralgia or neuritis, and disturbance of the abductors.

2. *Incomplete Fractures, Separation, or Displacement of the Epiphysis.* Traumatism more or less severe in character preceded the onset of the deformity in the case of Thiem, three cases of Manz, one case of Hoffa, and in two of my own cases. Thus the angle may be influenced by an incomplete fracture, separation, or displacement of the epiphysis with the consequent effect upon the growth of the epiphyseal line causing the growth to be greater on the inner side of the line carrying the head upward, or the growth to be greater on the outer side of the line carrying the head downward or inward, making the angle less. In one of my cases the traumatism acted in a manner never before observed—an injury inflicted by forceps applied to the breech.

3. *Rickets.* This group of cases includes those due to rachitis. Most writers on this subject agree that in some instances the bone softening preceding the deformity of the neck is the result of rachitis either infantile or adolescent. Hoffmeister and Grizel have reported cases and Albert observed one specimen.

4. *Osteomalacia.* In still other cases the softening process is simply a local manifestation of general osteomalacia. The deformity sometimes escapes detection on account of the bedridden condition of the patient, a factor which in itself tends to the production of an open angle.

5. *Osteomyelitis.* A specimen of coxa valga from osteomyelitis of the ilium has been observed by Albert. The bending of the bone must take place during the inflammatory stage.

6. *Exostosis.* Osteomata and the gouty material in arthritis deformans may, by acting as a wedge, cause coxa valga, as in one of my specimens.

7. *Tuberculosis.* Chronic inflammatory processes, of which tuberculosis is the most common, may produce coxa valga by local changes in the neck, as in the specimen in my collection.

Symptoms. *Clinical Picture.* The deformity develops insidiously, and being associated with or dependent upon other etiological factors, is not recognized until clearly established.

The attitude is characteristic; the contour of the hip is destroyed, and the buttocks flattened. There is slight flexion of the hip; external rotation of the thigh and knee, with eversion of the foot. The internal surface of the thigh looks forward and the knee is extended.

The essential features which are considered pathognomonic are the *abduction of the leg, associated with external rotation, and limitation of adduction.*

The first symptom which attracts attention is the peculiar gait. In the congenital case reported by David the child was late in walking and the abnormal gait was noticed at the time the child first attempted to walk.

In acquired cases the gait develops so gradually that its onset cannot be definitely determined, but may be from several months to several years after the advent of the fracture or joint disease or paralysis which was the existing cause.

In unilateral cases there is a decided limp due primarily to the inequality of the extremities, and the abducted and outward rotated position of the femur.

When the deformity is bilateral the upper part of the body is swung toward the side of the moving leg—a wavering gait, or, as David describes it, "an alternate swinging of the upper and lower parts of the body, which is so characteristic of the gait of sailors."

The gait resembles spastic paraplegia more than congenital dislocation—the feet being raised only slightly from the ground, one leg being bowed forward before the other foot is set down. The causative factor of the swinging gait is the abduction. The patient fatigues more easily than formerly, and pain and soreness is experienced about the hip-joint, particularly in the abductors and glutei muscles from the immoderate effort of these muscles to keep the pelvis horizontal.

Adduction is painful and there is sometimes a painful spasm of these muscles.

In bilateral cases the patient falls easily and raises himself up with difficulty, and can stand upon one leg only when supported.

Compensatory changes are shown in the trunk. In unilateral cases the upper part of the body is inclined toward the affected side, the shoulder on the sound side is lowered and there is lumbar scoliosis, the convex side being toward the affected limb.

In bilateral cases the normal lumbar lordosis is diminished and the upper part of the body is bent forward. Some

cases go on for years without detection and with slight inconvenience, while others seek relief from the increasing deformity and total disability.

Objective Symptoms. The deformity being local in character there is no relation between the general physical development and the deformity unless it be associated with rickets, or osteomalacia, etc. Atrophy of the muscles of the affected part is not marked.

Examination of the affected hip shows the contour changed by the displacement of the upper part of the femur. The great trochanter is anterior to its normal position and is lower than usual, a fact which can as a rule be demonstrated by palpation.

This lowering of the great trochanter destroys the isosceles of Byrant's triangle, as Gangolphe has demonstrated in his case. The trochanter may also be shown to be on or below Nelaton's line. The head of the femur is forward and its axis anteroposterior. The head may sometimes on deep pressure be felt to be within Scarpa's triangle.

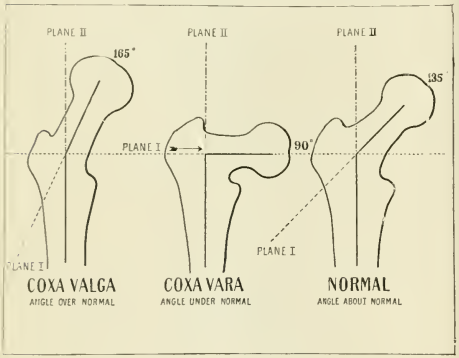

Fig. 7.—Original diagrams of angle of depression.

In the skeleton we have shown anatomical alterations in the angular relations between the femur and pelvis, and in the angular relations between the epiphysis and diaphysis of the femur, besides its other alterations. The angle formed by a plane passing through the long axis of the neck of the femur and a second plane passing through the vertical median line of the body is exaggerated in coxa valga. The angle formed by a plane passing through the pelvic bones and a second plane passing through the long axis of the diaphysis of the femur is also exaggerated.

In alterations between the epiphysis and diaphysis of the femur we may employ three methods of measuring—the angle of depression, or the angle of declination, and the triangle of Alsberg. The angle of depression—so called by Mikulicz—is formed by two planes, one passing through the long axis of the epiphysis and a second, in longitudinal section, passing through the long axis of the diaphysis. The arc of the normal angle appears to me to average 130°.[1]

These measurements are in the adult, as in infancy the angle is greater, and in senility usually smaller. Sometimes even in marked cases of coxa valga the alteration in the angle of inclination is slight, owing to twisting of the neck of the femur upon itself.

The angle of declination is represented by two planes (in horizontal section): the first plane passes transversely through the shaft of the femur, dividing it into an anterior and posterior position; the second plane passes through the direction of the long axis of the epiphysis. These planes form an angle, which is approximately about 165°. The angle is directed forward and within. In coxa valga the great trochanter is anterior to the normal position and the long axis of the femoral neck almost anteroposterior. The angle may be diminished to about 110° (Gangolphe's case), and the angle is directed backward and without. In coxa vara the angle is directed forward and without, the great trochanter being posterior to normal. This angle is of course difficult of demonstration except diagrammatically, as it may only be shown by horizontal section of specimens.[2]

Alsberg's triangle is formed by a line passing through the long axis of the femur and its continuation, a second line passing through the long axis of the neck of the femur, and a third line on a plane passing through the base of the head and parallel to a notch in the head and its continuation. In the normal condition the triangle is approximately equilateral, the apex upward. The angle formed at the apex is called by Alsberg the angle of "elevation." In coxa valga there is a shortening of the third line, the apex upward, and in coxa vara the triangles are reversed and the second line shortened.

Abduction is easy and increased; adduction is painful and sometimes the knee cannot be brought inside of the median line. Flexion of the thigh upon the pelvis is interfered with, and the knee can seldom be made to reach the abdomen. There is an actual lengthening of the affected

[1] Hoffa gives 126° as the normal, Mikulicz 125°–126°, Lauenstein 126°–129°, Alsberg 128°, and other authorities increase this angle as high as 140°.

[2] While the statement here made is in general true many exceptions were met with in the examination of the specimens of coxa vara and coxa valga recorded in this paper. Specimens were encountered where marked coxa vara existed and the angle of declination was greatly diminished (10,591), the long axis of the femoral neck being exactly transverse. Others were examined where the angle of declination was greatly increased and the femoral neck retained the normal angle of inclination (10,386). These variations may be considered valuable as proving the rule.

limb between the pelvis and knee, and not between the trochanter and knee. The neck of the femur is longer than normal in coxa valga, and it is from this lengthening and from the increase of the angle of depression that the actual lengthening of the bone is due. In rachitic cases there may be a bowing of the femur affecting this increase.

The *x*-ray is the best method of demonstrating the existence of this deformity, but in some cases, owing to forward dislocation of the trochanter, the picture of the affected hip is not so clear as the other. The picture of both hips should always be taken, and the anterior position is best.

Treatment. Less attention has been paid to the treatment than to any other phase of the subject.

Utilizing Wolfe's transformation law, David succeeded in improving the angle of depression in his case 7° with a corresponding improvement in function, by fixing the hip in

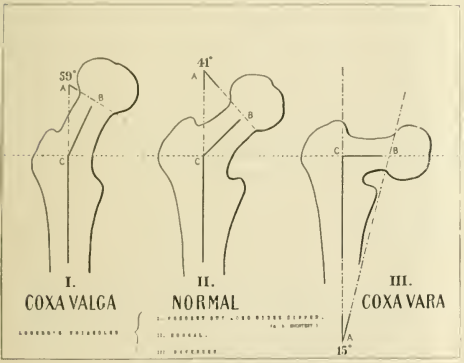

Fig. 8. Original diagrams of Alsberg's triangles.

a cast in an exaggerated position of adduction and inward rotation.

Two of my own cases were improved by tenotomy. In older cases equilization of the limb by the use of a high sole on the sound side will not only improve the gait, but will to some extent improve the angle of depression by changing the direction of the weight.

When the incipient stages have passed operative methods must be employed. An apparatus which would hold the leg in adduction with internal rotation would be of service during the incipient stage.[1]

In severe deformity with great disturbance of function, especially when associated with rheumatoid arthritis, a formal excision would be justifiable.

[1] Subtrochanteric osteotomy will be the operation of choice, and the bone should be retained in a position of marked adduction.

CASES OF COXA VALGA PUBLISHED PREVIOUS TO PRESENTATION OF THIS ARTICLE.

Case 1.—(Mauclaire, 1894 and 1895.) Coxa valga in scoliotics, especially in those having right dorsal convexity. The patient turns sideways to maintain the equilibrium, carrying the right limb in exaggerated abduction and rotation. If the lesion occurred before adolescence the femoral neck would probably be twisted. March, 1894, autopsy was made and showed an angle of declination of 110° in the anteroposterior axis of the femoral neck. Did not form an angle of more than 15° with the body. Internal rotation was impossible. Abduction was greatly limited. Also exhibition of other specimen.

Case 2. (Hoffmeister, 1894.) Case observed similar to Gangolphe's but his patient also exhibited signs of rachitis.

Case 3. (Grisel.) Case in a child aged four years, with rickets.

Case 4. (Theims, 1897.) Case following fracture, in a child.

Case 5. (Hoffa.) Case of traumatic coxa valga after fracture of neck.

Cases 6, 7, and 8. (Reichard, 1901.) Case after club-foot from anterior poliomyelitis. Trochanter major was 4 cm. below Nélaton's line. The trochanter minor was prominent.

Cases 7, 8, and 9. (Lauenstein.) One case due to rickets, two cases due to amputation stumps.

Case 10. (Gangolphe and Hau.) A man, aged twenty years, who had septic process in knee causing genu valgum. Had coxa valga on the other side, also due to septic process. Was unable to walk. Also had phthisis.

Case 11. (Hoffa.) Case following infantile palsy with both trochanters in Nélaton's line. Diagnosis made by *x*-rays.

Case 12. (David.) Boy, aged five years. No rickets, infantile paralysis, or injury. Early in 1903 was treated for progressive muscular dystrophy with pseudohypertrophy. October, 1903, was examined by David, who found both limbs markedly abducted, trochanter in Nélaton's line, and adduction and inward rotation diminished.

SPECIMENS MENTIONED IN LITERATURE.

Humphreys (1888) mentions 4 specimens from the Cambridge Museum in which the angle is given: 1 from hydrocephalus, the angle of each neck being 148°; 2 from paralytic limbs, the angles being 143° and 150° respectively; and 1 from a limb amputated from a lad, which it was inferred had not borne weight for some time prior to the operation, and in which the angle was 142°.

Albert mentions 8 cases: 1 associated with paralysis of the legs; 1 with weakness of legs but no paralysis; 1 with osteomyelitis of pelvis; 1 with rickets; 1 with osteomalacia; 1 with multiple exostoses; 1 with luxation of the other hip; and 1 with genu valgum.

Turner mentions 3 specimens: 1 from an amputation in early life, with an angle of 150°; 1 associated with tuberculosis of the ankle and knee; and 1 from fracture of the lower end of the femur with separation of the epiphysis.

Lauenstein notes 3 specimens with angles of 140°, 146°, and 155° respectively.

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EXPERIMENTAL AND PRACTICAL APPLICATION OF THE X-RAYS IN DISEASES OF THE BLOOD AND BLOOD-FORMING ORGANS, WITH REPORT OF CASES, AND A REVIEW OF THE LITERATURE ON THE SUBJECT.[1]

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The first object of this paper is to report the final results in one of the cases of leukemia, the case of pseudoleukemia and the one of polycythemia mentioned in the preliminary report last year, and to place on record a third case of leukemia, a new one of Hodgkin's disease, and one of pernicious anemia, together with the results of the metabolism investigations made in some of these and in other cases. Secondly, an attempt has been made to review the literature concerning the *x*-ray treatment of leukemia and pseudoleukemia, especially, but also of other diseases referable to the blood-forming organs, together with references to the practical application of the experimental researches upon the effect of *x*-ray exposures on the lymphoid structures in lower animals. Thirdly, the attempt will be made to show by these references, by the researches of Edsall and others in metabolism, and by statistics, that in leukemia, especially, the *x*-ray is not a curvative agent *per se*, but by secondarily destroying excessive and abnormal masses of lymphoid tissue, and greatly increased numbers of leukocytes in the blood, Nature, or, in other words, the individual organism itself, is given an opportunity to remove the cause. Lastly, a few instances will be cited showing that *x*-ray applications in certain grave constitutional disorders are not only dangerous and contraindicated, but may even cause death.

In the review of the literature, the following diseases have been included, and will be discussed in the order named:

Leukemia, both varieties.
Pseudoleukemia.
Polycythemia.
Splenic anemia.
Pernicious anemia.

This task has assumed greater proportions than was realized at the time I was asked to prepare a paper of this kind, and probably a few references have been overlooked. Literature does not reveal all of the cases that have been treated, and it would be safe so assume that not more than half the number have been reported. Many reports are included in discussions or published under titles that give no clue to their existence, and are therefore missed. Unfortunately it is not the custom to report failures, even though these are as important as are the successfully treated cases.

[1] Read before the seventh annual convention of the American Röntgen Ray Society, held at Niagara Falls, N. Y., August 29 to 31, 1906. Numerous additions have been made to the original paper.

LEUKEMIA.

Case I.—Last year I reported a case of splenomedullary leukemia successfully treated by the *x*-ray for a relapse following one year after a symptomatic cure under the administration of arsenic. Thirty-one exposures were made during a period of five and one-half weeks, and the patient went home apparently well, except that the spleen was still moderately enlarged. She was advised to submit to an occasional exposure as a prophylactic measure. Unfortunately, after the twenty-sixth application, she developed a dermatitis which resulted in a third degree burn that never healed entirely, and always interfered to a certain extent with subsequent treatment. Despite the fact that she received a few applications during the summer of 1905, she returned five months later (October 3, 1905) with a relapse. Treatment was started at once. At first the applications had no effect and the leukocyte count rose rapidly in ten days from 90,000 to 210,000. The spleen had increased to nearly its original size, but the general condition was better than when she returned home previously.

There were soon evidences of reaction, however, and the leukocytes began to diminish gradually. We were not able to bring about a symptomatic cure this time, and after thirty-six exposures, during a period of six and one-half weeks, she returned home November 19, 1905, to continue the treatment there. When she left, the leukocyte count was 33,400, the spleen was one-half inch below the costal margin (smaller than at any time) and her general condition was unchanged, or only about "fair." The trip home sent the leukocyte count up to 64,000 the next day, but they fell rapidly to 11,600 in five days, under treatment by Dr. G. C. Boughton, and the satisfaction of home surroundings. On December 4 the count was as low as 10,200. From then on there was a steady increase, and the last count made by Dr. Boughton was 77,000, on February 3, 1906. She returned to me for treatment of a fourth recurrence February 6, 1906. The spleen was considerably larger, the leukocytes numbered 95,000, and although she had gained in weight, she had lost in strength. *x*-ray treatment was started at once, and exposures of ten minutes each to the splenic area and three minutes to the knees were given almost daily. After twenty-six treatments, during a period of seven and one-half weeks, she returned home again, March 31, 1906. The spleen was no smaller, she was much weaker, and had lost considerable weight. The blood condition was: red cells, 4,180,000; leukocytes, 52,000; hemoglobin, 80 per cent. Myelocytes were still present. After returning home she gradually grew worse, and died June 14, 1906.

Case II.—H. A. E., male, white, nativity and residence Philadelphia, aged forty-three years, married, occupation saloon-keeper.

Family History. Negative; no tuberculosis or neoplasms.

Previous Personal History. Had diphtheria once. As is frequently the case in this disease, this patient gave the history of a severe malarial attack. This was eighteen or twenty years ago and lasted about eighteen months, confining him to bed part of the time.

History of Present Condition. In February, 1905, he had an attack of what was supposed to be "grip," and was in bed two weeks. He did not fully recover his strength and three months later he noticed a swelling in the left side below the costal margin. He took a trip to Europe but returned feeling worse. A diagnosis of splenomedullary leukemia was then made. Dr. Musser saw the case four months later and referred him for *x*-ray treatment, October 11, 1905. The patient's only complaint was weakness, but he was still able to work. The spleen was moderately enlarged and the leukocyte count was 96,000. *x*-ray treatment was started at once. Sixty-nine applications were made during a period of seventeen and one-half weeks, to February 10, 1906, when a symptomatic cure was apparent. The leukocyte count was then 4200, the spleen was not palpable, his general condition was apparently normal, his weight being up to his standard, and he felt as well as he ever had previously.

Unfortunately, no differential count was made to determine the presence of myelocytes. The leukocyte count began to rise slowly from this subnormal point, and on March 8 they numbered 6640. He returned in three weeks, as instructed, and the blood count (March 29) showed 16,000 white cells. From previous experience this was taken as an indication of the beginning of a recurrence, and *x*-ray treatment was resumed. In four weeks, after ten applications, the count was reduced to 11,000. From this time, May 24, the leukocytes again began to rise, and despite vigorous treatment it continued to do so, and by June 27, after eleven more exposures, they numbered 53,000. Then a reaction started, and there was a gradual irregular decrease to 14,600 at the last exposure before this report was made. During this relapse the spleen was palpable at times on deep palpation. The patient felt perfectly well during this entire time and continued to gain in weight. About 108 applications were made during a period of forty-three and one-half weeks, without producing a dermatitis, and this I ascribe to the use of the wet leather filter. This result is not to be looked upon as a cure, nor is a permanent result to be expected, in view of facts to be mentioned later in this paper, but every endeavor will be made to prolong the life of this patient in comparative comfort, just as long as the treatment tends to control the disease.

SYNOPSIS OF REPORTED CASES TREATED BY THE X-RAYS.

Splenomedullary.

Number.	Author.	Reference number.	Probable duration of disease	Effect of X-ray upon			Result.	Relapse.	Final outcome or present condition
				Spleen.	Leukocyter.	Relapse.			
1	Schultz	29	....	....	....	....	Symptomatic cure, 1904	....	Still well, 1905
2	Pusey	30	....	Enormous, not reduced	No effect	....	No effect, 1902	....	Died
3	Senn	31	....	" greatly reduced	64,800 to normal	No effect	Symptomatic cure, 1903	Relapse, 1904	Died*
4	Brown	32	6 months	Very large, to normal	800,000 to 7,894	No effect	Symptomatic cure, 1904	In one month	Died 10 weeks later, toxemia
5	Grosh and Stone	33	2 years	Enormous, slightly reduced	960,000 to 10,600	" "	Much improved, 1904	Acute relapse in a few days	Died
6	Bryant and Crane	34	....	Very large, to normal	176,000 to normal	" "	Symptomatic cure, 1904	Relapse 9 months	Died*
7	Evans	36	....	Enormous, slightly reduced	240,000 to 7,000, after becoming pregnant	Gradual rise to 70,000; x-rays had no effect	Improved, 1904	" following abortion, 1905	Died, April, 1906*
8	Weber	35	....	Enormous to normal	328,000 to normal	....	Symptomatic cure, 1904	Several relapses, this year a bad one	Not responding
9	Evans	36	....	Moderately enlarged to normal	250,000 to normal	Enormous spleen becoming smaller, 240,000, becoming less	Symptomatic cure, 1904	Relapse following pleurisy, 1905	Under treatment for relapse, Sept., 1906*
10	Cheyney	37	About 1 year	Enormous, to normal	126,000 to normal	....	Symptomatic cure, 1904		
11	Peacock	38	....	Much reduced under arsenic	692,000 to 54,000 under arsenic; 54,000 to 7,000 in 2 days under x-rays.	....	Treated 2 days only, with x-rays	....	Died
12	Dano	39	16 months	Enormous	128,000 to 37,000	Did not respond, spleen larger than at any time	Improved; stopped treatment July 11, 1904	Relapse in 2 months	Died Feb. 26, 1906*
13	Cahen	42	7 years	Very large, to normal	98,550 to 4,375	....	Symptomatic cure, 1904		
14	Joachim and Kurpjuwet	43	....	Enormous, somewhat reduced	693,000 to 6,300	....	Much improved, 1904	Relapse in 1 month	
15	Schleip and Hildebrandt	44	....	Enormous, slightly reduced	....	....	Improved; stopped treatment, 1905		
16	Hewlett	46	....	Enormous, somewhat reduced	400,000 to 40,000. Myelocytes not much reduced	Not treated since the fire	Improved; remained stationary several months after stopping active treatment, 1905	Feb., 1906. Hastened by an accident	Not treated or heard of since earthquake*
17	Lomme	48	....	....	....	....	Symptomatic cure, 1905	Relapse in 6 months	
18	Leddingham and McKerron	49	2 years or more	Enormous, greatly reduced	200,000 to 20,000	1st, 60,000 to 7000, 0; 2d, no effect	Improved, 1905	1st in 3 months; 2d immediately	Died
19	Krone	50	18 months	Became smaller and softer	Much reduced	....	Improved; still under treatment, 1904		
20	Ahrens	51	....	Enormous, to nearly normal	Reduced to normal	No effect	Symptomatic cure, 1904	Acute relapse in 2 months	Died
21	Aubertin and Beaujard	52	....	....	....	....	Improving; still under treatment, 1904		
22	Guilloz and Spillman	53	....	....	....	....	Improving; still under treatment, 1904		
23	Rodhe	54	....	....	....	....			
24	Fried	55	....	Much reduced	89,385 Still under treatment	....	Symptomatic cure, 1904		
25	"	"	....	Growing smaller	185,000 to 31,400. Still under treatment	....	Improving; still under treatment, 1904		
26	Schweinburg	56	....	....	....	....	Improved, 1904		
27	Soetbeer	57	....	....	....	....	Symptomatic cure, 1904		
28	Krause	58	....	....	320,000 to normal	....	Symptomatic cure, April, 1905		
29	"	"	....	....	156,000 to normal.	....	Symptomatic cure, April 1905		
30	"	"	....	....	220,000 to normal.	....	Symptomatic cure, April, 1905		
31	"	59	....	....	....	....	Symptomatic cure, April, 1905		
32	"	"	....	....	....	....	Symptomatic cure, April, 1905		
33	"	"	....	....	....	....	Not improved, April, 1905		
34	Eastman	63	....	Enormous, greatly reduced	1,110,000 to normal	No effect	Symptomatic cure, 1904	Acute relapse 18 months	Died 3 months later*
35	Bruce	64	4 months	Enormous, slightly reduced	400,000 to 32,000 (at time of report)	....	Improving; still under treatment Jan., 1906	Later, acute relapse	Died suddenly of intra-abdominal hemorrhage*
36	"	64	About 8 months	Enormous, slightly reduced	1,440,000 to 42,200 in 4 months	Up to 202,000 at time of report and reduced to 40,000, July, 1906; 142,000, Sept., 1906	Improved for 4 months, 1905	1st, 1905, improved; 2d, Sept., 1906	Under treatment, Sept., 1906*
37	Chester	65	About 8 months	Enormous, to nearly normal	244,500 to 12,600	No effect	Symptomatic cure, June, 1904	Relapse in 3 months	Died*
38	Holding and Warren	66	About 2 years	Enormous, somewhat reduced	....	150,000, Aug., 1906. Spleen larger than ever no effect from rays for over a year	Great improvement	Marked relapse Oct., 1905; treated to June, 1906	General condition no worse (will die)
39	Burdick	67	Several months	Tumor disappeared	150,000 to 8,000	No treatment	Symptomatic cure in 6 weeks, Jan., 1900	Relapse in 9 months; no treatment	Died*

40	Burdick	67	....	Very large, much reduced	85,000 to normal	Symptomatic cure	Symptomatic cure, 1900	Relapse in 1902	Still alive and well April, 1906*
41	"	"	6 months	...	...	....	Improved, 1903	....	Died Sept., 1903*
42	"	"	....	....	....	....	Improved	....	Died within 6 months*
43	"	"	....	....	....	....	Improved	..	Died within 6 months*
44	Smith and Capps	68	....	Much reduced	409,000 to 46,500	...	Improving, Oct., 1904	.	O
45	Melland	71	About 7 months	Enormous, much reduced	426,000 to 19,400	...	Much improved; still under treatment, April, 1905		
46	"	"	About 13 months	" " "	141,000 to normal	...	Much improved	.	Died—tuberculosis
47	"	"	9 months	Enormous, slight reduction	348,000 to 193,000	....	Improved; still under treatment, April, 1905		
48	"	"	8 months	" " "	542,000 to 90,000	....	" " "		
49	Eichberg	72	16 months	Enormous, much reduced; relapse; enlarged again	269,800 to 37,600	112,000, general condition still good	Much improved, June, 1906	Relapse Aug., 1906	Under treatment for relapse at present*
50	Schultz	73	2 months	Very large	289,000 to 134,000	...	Slightly improved at first	Later became worse	Died
51	Taylor	74	Several years	Very large to scarcely palpable	147,490 to 6,820	....	Symptomatic cure	Meningeal symptoms while under treatment	Died suddenly in 3 days
52	"	"	18 months	Very large—diminishing	127,000	..	Treatment just started		
53	Colombo	75	....	....	No effect	....	Not improved		
54	"	"	....	....	....	....	Improved		
55	"	"	....	Not reduced	96 000 to 440,000	..	Grew worse		
56	Elliott	76	....	Slightly reduced	160,000 to 68,000	...	Improving, but developed symptoms of spinal hemorrhage	....	Died in 5 weeks
57	Meyer	77	....	Very large, much reduced	152,000 to 2690	...	Symptomatic cure, 1905		
58	"	"	....	" " slightly reduced	120,000 to 140,000	..	Improved; patient stopped treatment		
59	Von Raake	78	....	.. ..	350,000 to 32,000 in 4½ weeks	.	Improving, 1905		
60	Thompson	80	2 to 3 years	Very large, slightly reduced	650,000 to 120,000	....	Improved; treatment stopped, but resumed later, 1905	....	Died of pneumonia, 1906 while under treatment*
61	Rosenberger	81	1 year	Very much reduced	234,000 to 13,800	..	Much improved	Quick relapse, Jan., 1905	
62	"	"	6 months	....	506,400 to 240,000	.	Improving, July, 1905	..	
63	Acuna	82	....	Not reduced	860,000 to 480,000	....	Improvement very slight	....	Died
64	"	"	....	....	350,000 to 95,000	No effect	Improved for 2 months	Relapse	Died
65	Beclere and Beaujard	83	21 months	Enormous, very much reduced	236,000 to normal	....	Symptomatic cure, July, 1905		
66	Haffman	84	....	....	109,000 to normal	..	Symptomatic cure, April 1905		
67	Ransom	85	3 years	Much reduced	160,000 to 6520, after a few exposures	....	Symptomatic cure, March, 1906		
68	Lossen and Morawitz	86	3 months	Very large, to nearly normal	315,800 to 9000	....	Symptomatic cure, June, 1905		
69	" " "	"	2 years	Enormous, not decreased Relapse, still larger	520,000 to 94,000	No effect; 130,000 at the start	Slight improvement	Relapse	Died
70	" " "	"		Treated a short time only					
71	" " "	"	....	....	.	....	Still under treatment, 1905		
72	" " "	"	....	....	..	....	" " "		
73	" " "	"	....	....	....	....	Improved		
74	" " "	"	....	....	....	....	"		
75	Eisenreich	87	....	Reduced to normal	165,000 to 6100	Not responding	Symptomatic cure	Relapse	Little hope of recovery
76	"	"	....	Decreased very little		" "	Improved	"	Little hope of recovery
77	Panconst	28	6 months	Enormous to nearly normal	407,000 to 6800	80,000 to 496,000; spleen slightly larger and not affected	Symptomatic cure, 1905	Acute relapse in 10 days	Died
78	"	"	18 months	Enormous, considerably reduced	304,000 to 9000	1st, 210,000 to 11,000; spleen nearly original size and much reduced. 2d, 90,000 to 52,000	" "	1st, in 5 months, improved; 2d, rapid and did not respond	Died
79	"	"	About 6 months	Enlarged to normal	96,000 to 5100	Still under treatment	Symptomatic cure	Slight relapse at present	Still under treatment
80	Pusey	104	Acute—5 weeks	Enormous, reduced to normal	160,000 to normal	....	Symptomatic cure in 1 month, Nov., 1904	None	Still well Aug., 1905
81	Bryant	L	....	....	....	..	Improved	Relapsed	Died
82	Eastman	L	....	Very little effect	....	....	Imdicated under treatment	.	Died suddly; cause unknown
83	Bruce	L	Probably several years	Reduced to nearly normal	280,700 to normal. (Red cells also dropped from 4,860,000 to 2,260,000)	....	Symptomatic cure in 1 month		Died 4 months later

* Final reports of cases received by letter from the authors of the original reports.

L Cases not reported in literature, but data received by letter. (Cases 81 to 83.)

O Final reports of these cases not obtainable at present on account of the absence of Dr. Smith, who is in Europe.

Lymphatic Leukemia.

Number.	Author.	Reference number.	Probable duration of disease.	Effect of X-ray upon: Spleen.	Leukocytes.	Glands.	Result.	Relapse.	Final outcome or present condition.
84	Sonn	24	10 years	Slightly enlarged; later became enormous (due to a toxemia from treatment)	208,000 to 46,500. (Later to normal)	Intra-abdominal and all superficial; also tonsils and liver. Reduced to normal	Symptomatic cure 1903; toxemia twice.	None	Living and well, Aug. 1906
85	Bozzolo	40	....	Enormous, much reduced	140,000 to 10,000	....	Symptomatic cure	Quick relapse, cured; 2d cured, 1905	
86	Schenck	41	7 years	Moderately enlarged, slightly reduced	140,000 to 32,000	....	" "	Relapse	Died
87	Joachim and Kurpjuwet	43	....	Very large, much reduced	500,000 to 30,000	Enlarged; somewhat reduced	Slight improvement	Tendency to relapse, Dec. 1904	
88	Pusey	45	1 year	Moderately enlarged to nearly normal	160,000	All superficial glands enlarged and nearly disappeared	Much improved	Relapse in 3 months, cured, 2d; acute	Died
89	Herz	47	....	....	....	Slightly reduced	....	....	Died (intercurrent pneumonia)
90	Preiss	61	Acute	Great enlargement	Blood count resembled pernicious anemia (may have been splenic anemia	Slight enlargement; not reduced	....	....	Died
91	"	"	3 years	Considerably enlarged	....	....	Still under treatment, 1905		
92	Grawitz	62	....	Very large, much reduced	1,250,000 to nearly normal	Much reduced	Marked improvement, 1904		
93	Burdick	67	....	....	....	....	Symptomatic cure in 3 months, 1900	Relapse in 6 months. Not treated	Died*
94	"	"	....	....	....	....	Symptomatic cure in 4 months, Jan., 1902	Relapse; not treated	Died same year*
95	"	"	....	....	....	....	Symptomatic cure, 1902	Slight relapse, 1904 and again cured	Living and well today (4 years)*
96	Smith and Capps	68	Acute, 1 month	No effect	No effect	No effect	Treated 6 days only	....	Died
97	" " "	"	Acute		69,000 to 299,000	" "	" 10 " "	....	Died
98	" " "	"	Acute	Slightly reduced	12,000 to 3000	" "	" 7 weeks	....	Died
99	" " "	"	Subacute, 4½ months	No effect	80,000 to 64,000	" "	" 6 "	....	Died
100	" " "	"	" " —1 year	Much reduced	70,500 to 25,000,	Reduced to nearly normal	" 10 months	....	Died
101	" " "	"	Chronic, 2½ years	Reduced to nearly normal	295,000 to 6800	" " " "	Almost symptomatic cure	....	Died in 1 month
102	" " "	"	26 months	Reduced to nearly normal	150,000 to 4200	" " " "	Symptomatic cure		Living Sept., 1905 O
103	" " "	"	2½ years	Much reduced	300,000 to 12,000]	Much reduced	Much improved	Relapse, 1905	O
104	" " "	"	14 months	" "	145,000 to 6000	" "	" "	....	Living Sept., 1905 O
105	" " "	"	15 "	"	164,000 to 16,000	None present	" "	....	Living Sept., 1905 O
106	" " "	"	....	Slightly reduced	350,000	Slightly reduced	Slightly improved; patient stopped treatment after 3 weeks	....	
107	" " "	"	14 months	Much reduced	210,000 to 25,000	Markedly reduced	Improving	....	Died suddenly
108	Gray	69	Subacute	" "	140,000 to normal	Much reduced	Symptomatic cure in 7 weeks	....	Died 4 weeks later
109	Dock and Warthin	70	....	Very large, slightly reduced	60,000 Reduced for a while, but rose again	Great enlargement of all, much reduced	Slightly improved at first	....	Died rather suddenly—intoxication
110	Grad	79	1 year	Much reduced	234,000 to 13,800. Relapse, 139,200	Much reduced	Much improved	Relapse in 2 months	Died*
111	Beclere and Beaujard	83	3 years	Enormous, to nearly normal	285,000 to 4200	Enormous, reduced to nearly normal	Symptomatic cure, 1905		
112	Krause	60	....	....	....	....	Improved only, 1905		
113	"	"	....	....	....	....	" " "		

Unclassified Cases.

114	Hoffmann	"	....	....	....	....	....	....	Died soon after beginning treatment
115	"	"	....	....	....	....	....	....	Died soon after beginning treatment
116	"	"	....	....	....	....	....	....	Died soon after beginning treatment
117	"	"							
118	Wendel	88							
119	Schieffer	89	....	....	....	....	Symptomatic cure, 1905		
120	"	"	....	....	....	....	Improved by a few exposures and stopped treatment		
121	"	"	....	....	....	....	Improved at first	Relapse soon	Died
122	"	"	....	....	....	....	Symptomatic cure, 1905		
123	"	"	....	....	....	....	" " "		

* Final reports of cases received by letter from the authors of the original reports.

O Final reports of these cases not obtainable at present on account of the absence of Dr. Smith, who is in Europe.

The record of the leukocyte counts in detail follows: November 2, 1905, 44,000; 9th, 56,000; 16th, 56,000; 23d, 51,000; December 15th, 31,000; 22d, 26,400; 28th, 21,000; January 4, 1906, 19,500; 12th, 15,200; 19th, 14,400; 25th, 10,200; February 8, 6200; 10th, 4200 (treatment stopped); 22d, 5100; March 1st, 6280; 8th, 6640; 29th, 16,000 (treatment resumed); April 5th, 10,600; 12th, 20,400; 17th, 12,400; 10,270; 42th, May 4th, 12,000; 8th, 14,000; 16th, 14,200; 20th, 12,560; 24th, 11,200; 27th, 12,960; June 6th, 14,000; 9th, 15,200; 11th, 15,760; 16th, 22,000; 18th, 21,200; 20th, 23,560; 22d, 30,640; 24th, 19,000; 27th, 53,000; 29th, 57,500; July 1st, 41,660; 2d, 23,000 (no treatment since June 27); 5th, 24,660; 7th, 25,000; 9th, 23,300; 11th, 22,600; 13th, 22,000; 16th, 20,600; 18th, 27,300; 20th, 17,600; 23d, 22,600; 25th, 18,300 (changed to a harder and black tube); 27th, 13,600; 30th, 24,300; August 1st, 21,500; 3d, 15,000; 6th, 14,600.

At the present time (November 15, 1906) this patient has still another relapse. Although the leukocytes had shown a tendency to rise ever since he came home from a camping trip in the South, about a month ago, they could be held in check by one exposure every five days. About ten days ago he had a series of chills and slight rises in temperature for three or four successive days accompanied by gastric disturbance, slight pain, and weakness in the lower extremities and a tendency to sweating. The spleen enlarged rather suddenly, and extended about two inches below the costal margin. The leukocytes showed a greater tendency to increase than before and an exposure is required every three days to hold them in check. A full blood examination was made on the above date by Dr. Laird, and was as follows: Erythrocytes, 4,080.000; leukocytes, 38,000; hemoglobin, 82 per cent.; polymorphonuclears, 50 per cent.; lymphocytes, 5 per cent.; transitionals, 1 per cent.; myelocytes, 44 per cent.

The urine examination was negative.

Although the leukocyte count is not excessively high, it will be noted that there is a high percentage of myelocytes. Two months ago, before he went away on his trip, they constituted but $2\frac{1}{2}$ per cent. of the white cells. Under the circumstances, it would be far more gratifying to me to see a leukocyte count of 100,000 with a lower percentage of myelocytes than the existing condition of the blood. While this patient's general health is at its best, it seems possible to hold the disease in check, but any indiscretion in diet, or "catching cold," or any trifling disturbance of this kind seems to bring forth evidence that the etiological factor is still present. I am satisfied that the ordinary *x*-ray technique is not sufficient for our purposes, and several experimental changes are being tried at present with this patient. He has improved somewhat in the past few days.

In reviewing the literature on leukemia, references have been found for 120 cases in which *x*-ray treatment was employed. This number must represent nearly all the reports up to September 1, 1906. In reply to letters sent out for the purpose of obtaining the subsequent history and final outcome of cases previously reported, the writers have mentioned a few additional ones, and these will be included in the summary. Lack of time has prevented the perusal of many articles on this subject, but numerous references will be found in the bibliography at the end of this paper.

Summary.

Splenomedullary cases reported in literature	80
Splenomedullary cases reported by letter	3
Lymphatic cases reported in literature	30
Unclassified cases reported in literature	10
Total	123

The primary results obtained by the treatment were as follows:

	Spleno-medullary.	Lymphatic.	Unclassified.	Totals.
Symptomatic cure	33	11	3	47
Improved	22	8	2	32
Improved and still under treatment	14	1	0	15
Not affected or but slightly improved	13	10	3	26
Report of result not obtained	1	0	2	3
Totals	83	30	10	123

Of the 123 cases included in the table, final reports have been received or found of 63, or slightly more than 51 per cent. The following table shows the final outcome or present condition of these patients:

	Spleno-medullary.	Lymphatic.	Unclassified.	Totals.
Still living and well	2	2	0	4
Symptomatic cure, relapsed, died	11	5	0	16
Symptomatic cure, relapsed, living, but condition very grave	5	0	0	5
Improved, relapsed, and died of the disease or an intercurrent infection	14	3	1	18
No effect, or but slightly improved, and died	5	8	3	16
Symptomatic cure, relapse, and under treatment at present time	4	0	0	4
Totals	41	18	4	63

By referring to the above table, it will be seen that out of the 63 cases mentioned, only 4, or 6.35 per cent., are still alive and well three to six years after the primary symptomatic cure. It is safe to assume that were the final reports at hand of all cases that have been treated by the *x*-ray, this percentage would not be altered to any great extent. By including with those cases which have died 5 which were symptomatically cured, but now are in a critical condition, and will undoubtedly die soon, the death rate is 55, or 87.3 per cent. The remaining 4 cases, or 6.35 per cent., are at present under treatment for relapses

following symptomatic cures. It will be noted that in 39 cases, or over 70 per cent. of those that died or are at present in a critical condition, there was either a very marked improvement in the symptoms, or a symptomatic cure, as a result of the treatment at first. Those cases which did not respond to the treatment, or were but slightly affected, were less than 30 per cent.

One case of splenomedullary leukemia reported by Schultz[29] as symptomatically cured in 1901, was still well without relapse in 1905. Burdick's[67] case of the same variety was symptomatically cured in 1900, had a relapse in 1902, but recovered and was still alive and well in April, 1906. Senn's[31] case of lymphatic leukemia was cured in 1903 and was still alive and well August, 1906, without a relapse. Burdick's case of the lymphatic variety was symptomatically cured in 1902, had a slight relapse in 1904, but recovered and was still well in August, 1906.

Dr. H. E. Potter, of Chicago, has advised me of 1 unreported case of acute lymphatic leukemia (with a leukocyte count of 1,150,000) and 2 of the splenomedullary variety now under treatment. Dr. Eastman is treating 1 splenomedullary case, which is responding well, and Dr. E. G. Williams has just started treatment on another, with early improvement.

The cause of death in some instances is worthy of mention. It is possible to select at least a dozen cases in which a toxemia has brought about an early or sudden termination. One notable example is Peacock's[38] patient, who was progressing favorably under arsenic with a reduction in leukocytes from 692,000 to 54,000. Two *x*-ray exposures were then made, resulting in the death of the patient in two days. The leukocytes dropped in this time from 54,000 to 7000. Eastman has reported, personally, that his patient died suddenly of unknown cause. Dock and Warthin's case is acknowledged to have died of toxemia induced by the treatment. Brown's[32] case died as a result of intoxication, and an interesting autopsy followed, and will be referred to later in connection with the one on Dock and Warthin's patient.

Evans' first case reported as improved, later had a relapse following an abortion and died. His second case, cured in 1904, had a relapse the next year following an attack of pleurisy, and is at present still under treatment. Bruce[64] reports, personally, that his case after showing great improvement had an acute relapse, and died suddenly of intra-abdominal hemorrhage. Melland's[71] case is said to have died of tuberculosis after improvement in the leukemia symptoms. Taylor[74] obtained almost a symptomatic cure in his patient, but while still under treatment, death occurred in three days after development of meningeal symptoms. Elliott's[76] case died after developing symptoms of spinal hemorrhage. Thompson[80] and Herz[47] each had a patient die of intercurrent pneumonia while under treatment.

In connection with these facts it may be remembered that intercurrent infections are frequently responsible for spontaneous improvements in leukemia and pseudoleukemia. Neutra,[103] in 1903, had collected 19 recorded cases in which there was a marked reduction in leukocytes during and after an intercurrent infectious disease. He stated that there was never any improvement in the general condition, however, and believed that the reduction was due to a destruction of leukocytes by the toxins of the intercurrent disease and not to any improvement in the leukemia.

The results of the Röntgen-ray treatment of leukemia are certainly not very encouraging. In view of the high death-rate, the frequency of relapse, and the results of experimental research, the *x*-ray cannot be regarded as a specific therapeutic agent in either variety of leukemia. Although its influence in rapidly destroying enormous numbers of leukocytes in the blood, in reducing a spleen of tremendous proportions to a normal or nearly normal size, and likewise similarly affecting the enlarged lymph glands, is obvious to all of us, nevertheless, the true cause of the disease is evidently not destroyed and a relapse is sooner or later to be expected. However, the mortality is no higher than by any other form of treatment, and we can usually be reasonably certain in a case not too far advanced of at least prolonging life, and there is a slight chance of the patient remaining free from symptoms for a number of years, if not of being permanently cured. It seems to be accepted generally that no case of splenomedullary leukemia can be considered cured while myelocytes are still to be found in the blood.

The dangers attending the use of the *x*-ray as the therapeutic agent should be well borne in mind, and not only should evidences of toxemia be looked for, but careful examinations of the urine should be made frequently to determine, approximately, the extent and rapidity of tissue destruction and the state of the kidneys. The evidences are very numerous in literature of death having been caused or hastened through failure to observe these points.

Because of the autopsy finding in a few cases of leukemia it has been claimed that the *x*-rays may have a degenerative action upon the kidneys during the treatment of such conditions, but there are no facts mentioned in literature to substantiate this belief. The pathological changes observed in the kidneys in the few cases that have gone to autopsy were in all likelihood due secondarily to the *x*-rays through the increased work imposed by the elimination of waste tissue products and toxins, and would really be expected in view of the clinical phenomena. At the last meeting of the American Röntgen Ray Society, in August, 1906, Warthin[106] read a paper on the autopsy findings in 2 cases of leukemia that died while under treatment, and in each of which the clinical phenomena of a toxemia were manifest

at the time. One of these was Warthin's own case, and the other was reported by E. J. Brown.

The case treated by Brown was one of splenomedullary leukemia with a very large spleen and the following blood picture: red cells, 2,600,000; leukocytes, 800,000; hemoglobin, 65 per cent.; myelocytes, 40 per cent.

The patient was treated about ten months and received over 100 exposures. For the first two months of *x*-ray treatment, iron and arsenic were administered in conjunction, and the leukocytes were reduced to 58,000. A symptomatic cure resulted inside of one year with the following blood picture: red cells, 4,690,000; leukocytes, 7894; hemoglobin, 90 per cent.; myelocytes not recorded.

There was a relapse in one month and the treatment then seemed to have no effect. There was every evidence of an intoxication and the symptoms resembled those of typhoid fever. The patient died in ten weeks. One of the most important and interesting facts determined at the autopsy was the condition of the kidneys. There were evidences of acute interstitial inflammation and marked necrosis of the epithelium of the tubules. Numerous small deposits of lime salts were found in the tubules. It is said that the postmortem appearance resembled that which might be found in a case of acute mercurial poisoning. In this case there had been evidences of nephritis before the treatment was started.

The case reported by Dock and Warthin, one of lymphatic leukemia, had marked enlargement of all the superficial glands, especially the cervical and axillary. The spleen was very much enlarged and the leukocytes varied from 40,000 to 60,000, small mononuclears predominating. At first the general condition improved, the glands were considerably reduced, and the leukocytes were reduced somewhat. Later the patient failed to respond to the treatment and the general condition became worse, the leukocytes increased and death occurred rather suddenly. Symptoms of intoxication preceded death. The autopsy showed that all the organs, and especially the liver, were infiltrated by lymphatic tissue. There was a large retroperitoneal lymphoid mass resembling sarcoma. The kidneys resembled those of Brown's case.

Some importance should be placed upon the fact that in a large number of the fatal cases of both leukemia and pseudoleukemia either the autopsy or the clinical symptoms before death have revealed the presence of deep-seated lymphoid deposits that have not received their share of the exposures, probably because they escaped notice in the early part of the treatment. It has often happened that a relapse in Hodgkin's disease has shown itself by lymphatic enlargements in entirely new areas from those previously treated.

Although it has not been proved with absolute certainty that the action of the *x*-ray as a therapeutic agent in leukemia is exactly the same as Heineke and Warthin have demonstrated as the effect of the rays upon the lymphatic tissues of healthy animals, there is, however, sufficient evidences in literature to give ample support to this theory. Three theories of any importance have been advanced. At first Senn and Ahrens claimed that the rays probably actually destroyed or inhibited the development of a *hypothetical* parasite of leukemia. A second explanation of the phenomena was that the *x*-ray exerted an inhibiting action upon the blood-making organs and did not cause a destruction of cells in these organs. The theory that the destruction of the leukocytes (existing in an abnormal state both as to numbers and structure) and abnormal deposits of lymphoid tissue is due to the stimulation of an autolytic process, through some action of the *x*-ray, seems to have been sufficiently well demonstrated by competent authorities to be accepted. A *resume* of the investigations of Edsall,[113] based upon those of Heineke and Warthin, was included in my paper[28] read last year. Lossen and Morawitz[86] reported two cases in which metabolism investigations were made, similar to those made by Edsall. In the first instance the investigations were carried on at the beginning of the treatment of a case of splenomedullary leukemia. The average elimination of nitrogen, uric acid, and P_2O_5 during the first sixteen days of treatment fell below that of the ten days preliminary control period, although on some days there was an increase. This patient was symptomatically cured. In the second case the investigations were made at the beginning of the treatment of a relapse. The exposures had very little influence upon the general condition, although the spleen was greatly diminished and the leukocytes were considerably reduced, from 501,000 to 367,000, during the metabolism investigation period of eight days. The elimination of nitrogen increased about 40 per cent., uric acid about 57 per cent., and P_2O_5 about 130 per cent. As death approached the elimination fell gradually below the average of the preliminary control period, even though there was a daily reduction in leukocytes and in the size of the spleen. Evidently the kidneys were not eliminating the waste products. Numerous uric acid calculi were found in the kidneys at autopsy. Rosenberger[25] arrived at the same results in his investigations, and in addition found that the elimination of waste tissue products did not increase to any extent during the *x*-ray treatment of *pseudoleukemia*.

There is no definite knowledge as to who was the first Röntgenologist to apply the *x*-ray as a therapeutic measure in leukemia. A recent letter from Dr. Burdick, of Chicago, states that he obtained a symptomatic cure in a case of the splenomedullary variety as early as 1900, and that this patient is still alive and well. He also states that he cured a case of lymphatic leukemia in 1902. In the preparation of this article much assistance has been rendered by the

recent valuable paper by Dr. Eichberg.[72] He calls attention to the fact that Schirmer (references 29 and 101) refers to a case of leukemia cured by Schultz in 1901, and which was still well four years later. Only those who have reported their cases, however, should receive the full credit, and the first report of a leukemic patient treated by the *x*-ray was made by Pusey[7] in April, 1902. The case was one of the splenomedullary variety and did not respond to the treatment. Senn[31] was the first to report a case successfully treated in August, 1903.

There are several recorded instances in which splenectomy has been resorted to as a therapeutic measure in leukemia. Lindner[107] reported 1 case which was much improved, but cured, and refers to 4 reported cases in which there were symptomatic cures, and 28 in which there was no benefit. Richardson[108] reported a case upon which he operated and presumably obtained a symptomatic cure in 1900, but the patient died in 1904. According to his last report he does not think that the first result was due to the operation, but to the medicinal treatment employed. In his conclusions in regard to the value of surgical interference in this disease, he expresses the following opinion: "A disease in which successful extirpations of the spleen are so unusual—in which almost the only successful operation has been followed after temporary improvement by a distressing death—such a disease must by common sense be removed from the category of surgical affections, even if there is, as in one case, no positive proof that the final bad result is directly dependent upon the operation itself."

PSEUDOLEUKEMIA.

Case V.—Puesdoleukemia. M. P., male, forty-two years, married, native of Austria, occupation store clerk. Referred by Dr. M. H. Fussell, medical dispensary.

The patient was admitted to the dispensary September 26, 1904.

Family History. Negative. No tuberculous history.

Previous History. None of the diseases of childhood. He has suffered with dyspepsia for twenty-two years, and attributes this to fasting for three months, eating only a loaf of bread one day during each week in order to reduce his weight below the standard, and thus avoid army conscription. After this fast he had an abnormal appetite which has continued more or less ever since. About seven years ago he began to have trouble with his foot, and about eighteen months ago he received 21 *x*-ray applications, and was cured, and has had no further trouble with it. He says he was told he had a sarcoma of the skin.

History of Present Trouble. For a year he has been feeling weak and has been confined to bed several times in consequence, and on account of dyspepsia. Six months ago he consulted a stomach specialist, who did nothing for this condition, but discovered that the spleen and the cervical axillary and inguinal lymphatic glands were enlarged, and the blood examination revealed an anemia. He was treated with bone-marrow and arsenic for about a month, and the glandular swellings disappeared. During the past week the spleen and glands have again enlarged.

Condition on Admission. Complains of weakness, slight dizziness, dyspepsia, œdema of the ankles, and puffiness of the lower eye-lids at times. No dyspnœa, appetite good, bowels regular. The tongue is heavily coated. The urine contains a trace of albumin but is otherwise negative. Considerable œdema of the legs and ankles, which is less in the morning. The thorax is negative except for a possible impairment of resonance over the right apex. The *spleen* extends from the eighth rib in the midaxillary line, above, to an inch and a half below the costal margin, and is movable. The stomach is ptosed and by inflation extends downward to the umbilicus. The right kidney is movable. The liver is not enlarged. All superficial lymphatic glands are enlarged as follows: Submaxillary, the largest, size of a walnut; postcervical, slightly; supraclavicular slightly; both axillæ and epitrochlear, latter the size of a pea; both inguinal, size of a lima bean; one gland on the dorsum of the penis behind the corona, the size of a large pea, but flat; one gland in the right popliteal space (this appeared or was discovered later on).

Treatment. Arsenic and bone-marrow, continued one month.

Blood Chart. September 26, 1904. Red cells, 3,700,000; leukocytes, 4400; hemoglobin, 35 per cent. Differential count: polymorphonuclears, 61 per cent.; small mononuclears, 25 per cent.; large mononuclears, 14 per cent.

October 10*th*. Red cells, 4,510,000; leukocytes, 17,000; hemoglobin, 55 per cent.

11*th*. Leukocytes, 16,300; hemoglobin, 50 per cent.

27*th*. Red cells, 4,660,000; leukocytes, 10,200; hemoglobin, 55 per cent., after large meal. (10 *x*-ray exposures.)

November 1*st*. Red cells, 4,500,000; leukocytes, 6720; hemoglobin, 60 per cent. (several hours after meal).

February 7, 1905. Red cells, 5,200,000; leukocytes, 7200; hemoglobin, 90 per cent. (67 *x*-ray exposures.) Differential count: Polymorphonuclears, 53.5 per cent.; small mononuclears, 25.5 per cent.; large mononuclears, 12 per cent.; eosinophiles, 5.5 per cent.; basophiles, 3.5 per cent.

September 1*st*. Red cells, 4,930,000; leukocytes, 8880; hemoglobin, 80 per cent. (104 *x*-ray exposures.)

x-ray treatment was started October 7, 1904, and during the remainder of the year forty-eight applications were made. Each time the tube was placed over the abdomen, then over the thorax, including the axillæ and one side of the neck, and then over the inguinal regions. The exposure over each area lasted two to five minutes, with the anode fourteen

to sixteen inches from the skin. These exposures may seem short, but in reality they were severe,* as an electrolytic interrupter was used, and a primary current of from 5 to 15 ampères, forcing a secondary current of from 1 to 2 milliampères through a hard tube with a vacuum equivalent to 3 to 5 inches of spark gap resistance. It was known that the superficial glands would absorb fewer rays than from a softer tube, but they evidently absorbed enough, and we were after the deep-seated glands that must also have been enlarged. Later, when a mechanical spring interrupter and less primary current were used the exposures were made longer. After receiving these forty-eight applications all the superficial enlargements except the nodule on the penis were considerably reduced in size. The spleen varied and the changes in size were rapid, an increase in size being usually accompanied by an attack of indigestion. From January 4, 1905, nineteen additional applications were made up to February 7, when the only glands still enlarged were the postcervical (slightly), the left parotid lymphatic, and the inguinal, which were still considerably enlarged. The nodule on the penis remained the same. The stomach was still ptosed, and the liver also, but it was not enlarged. The spleen extended from the ninth rib above to the level of the umbilicus below, but could be pushed up under the costal margin, and then the splenic dulness extended upward to the eighth rib. The general condition was considerably improved. Treatments were continued three times a week until March 31, 1905, making twenty-one additional applications. These were made as often and as severe as the skin would allow. From this time until May 12 there were ten exposures, or two a week. He then developed a mild erysipelas of the right leg accompanied by a marked enlargement of the saphenous glands. This condition subsided in about ten days and treatments were resumed May 23, and continued once a week until July 3. The spleen was then larger, and he had suffered from indigestion for two weeks. He did not return until August 5, and was then feeling much better, and a few days later the spleen was barely palpable. From this time until October he came back but three times and has not been seen since. At the time of the last visit the spleen was nearly normal in size, most of the glandular enlargements had disappeared, and those remaining were much reduced in size, but both the spleen and glands varied at intervals. He had no cough but a slight dulness was found at the right apex, and he had some pain in the right side of the chest. There was puffiness of the lower lids. His weight was 127½ pounds, 130 being normal. He was emaciated in appearance but was probably always so, and the skin was sallow. On account of his weakness it cannot be said that the general condition had improved as much as the blood examination would seem to indicate. In all, he received 107 *x*-ray treatments during a period of one year.

We cannot record this case as a "cure," and the most that can be said is that we brought about a considerable improvement, symptomatically. Evidences of the disease certainly still remained and whether or not the general condition was due to phthisis or to the splanchnoptosis and accompanying gastric disorder cannot be stated definitely. I hardly believe that the patient is still living, but if he is, he has either gone to another institution for treatment, which is not likely, or is to be considered a hopeless invalid.

Case VI.—Pseudoleukemia. Mrs. A. W., aged forty years, native of Pennsylvania, married. Referred by Dr. J. M. Spellissy.

Family History. Negative; no neoplasms, anemias, disease of the thyroid, nor tuberculosis.

Previous History. Negative.

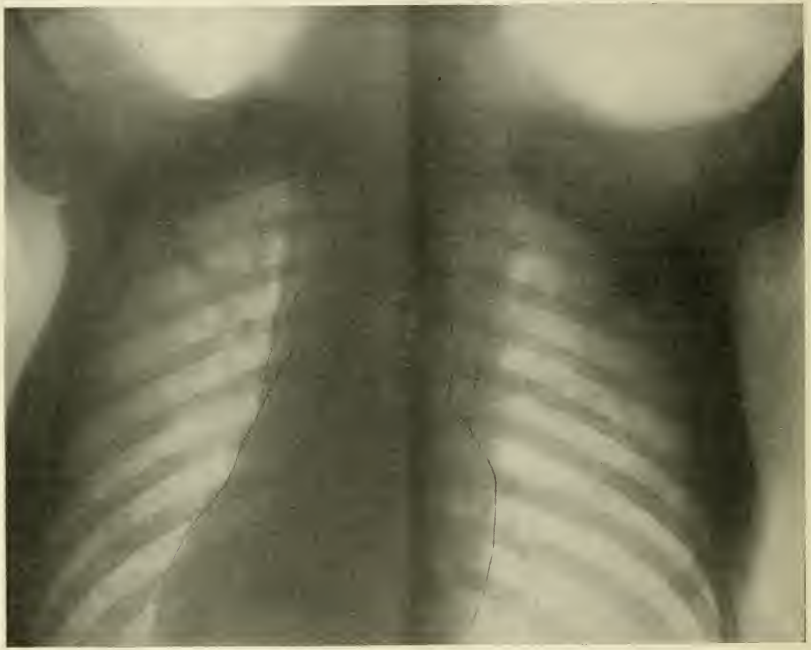
History of Present Condition. In November, 1905, the patient noticed a swelling in her neck over the suprasternal notch. It was painless and soft at first but grew progressively, upward and to the right, and became firmer, and soon began to cause difficulty in swallowing and breathing. She began to lose weight and strength about the time the swelling was noticed. In March, 1906, the pressure had become so great that she could not lie down on account of dyspnœa, and could swallow soft food only. By this time she had lost thirty-five pounds in weight. On March 12, she was operated on by Dr. Spellissy for what was supposed to be a malignant growth of the thyroid, or cervical lymphatic glands, or possibly a local manifestation of Hodgkin's disease. The mass in the neck was removed partially under local anesthesia, as a general anesthetic was contraindicated on account of the dyspnœa. After incising the neck, a chain of dense lymphatic glands lying upon the internal jugular vein was removed from the mastoid process to about one and one-half inches below the sternal notch. The opening up of the neck relieved the dyspnœa and the operation was finished under ether. Below this mass and an inch and a half below the sternal notch, glands of the same character were felt but could not be removed without splitting the sternum, and their further treatment was deferred until the pathologist's report should be received. Dr. Longcope examined the specimen and pronounced the growth to be a localized lymphatic enlargement due to pseudoleukemia. It was then thought advisable to submit the patient to *x*-ray treatment.

I saw her three weeks later and concurred in this opinion, as it seemed to offer the only chance, though a remote one,

* While Dr. Edsall was carrying out his metabolism experiments on the case of unresolved pneumonia mentioned later in this paper, we found that the exposure of a few seconds while making a skiagraph was almost as effective as the ten-minute therapeutic applications in which the rays were generated by much less volume of current and slower interruptions.

of curing her, but would at least probably prolong her life. There was a sinus still persisting in the line of the scar and probably due to a lateral ligature of silk on the jugular vein. Immediate treatment was advised but the patient felt much better and wished to return home first, promising to come back in a few days. She did not return until June 27, fifteen weeks after her operation. About the end of April, or six weeks after the operation, she noticed a recurrence of the growth in the suprasternal notch, and it grew steadily upward and to the right, and soon caused a return of pressure symptoms. When she returned to me the mass was about the size of an egg and firm and immovable. It was necessary for her to sleep in a semi-recumbent posture on account of extreme dyspnœa, and she could swallow soft food only. The right pupil was dilated. She was again losing weight. Examination of the chest revealed dulness over both apices and extending farther down on the right side. The skiagraph (see illustration) made July 8 shows the extent of the intrathoracic portion of the growth.

A single *x*-ray exposure was given June 27, and then after consulting with Dr. Ralph Pemberton it was decided to carry out Dr. Edsall's metabolism investigations on this case, which seemed particularly suitable on account of the very large and localized mass. From this date until July 4 "placebo" applications were made with a punctured tube, as it was necessary to have a preliminary control period on the special diet without *x*-ray exposures before the treatment was begun in earnest, and the patient was unwilling to submit to any delay. She was admitted to the University Hospital on the service of Dr. Tyson, June 29, and was



Pseudoleukemia, Case VI. The solid lines indicate the limits of the cardiac and aortic shadows laterally. The shadow above the heart and extending to each side and above the aorta represents the mediastinal growth at the time treatment was started, July 8, 1906. The broken lines indicate the extent of the growth laterally as shown by the last skiagraph made December 6, 1906. By measurements on the two skiagraphs, it was found that the growth had diminished from five-eighths to one-half an inch in breadth. As the growth is mainly in the anterior mediastinum and the exposures were made with the plates back of the patient, the shadows are wider than the growth itself.

at once placed on the special diet used in the investigations in the leukemic cases previously reported. The blood examination showed: red cells, 4,880,000; leukocytes, 7760; hemoglobin, 55 per cent.; polymorphonuclears, 82 per cent.; lymphocytes, 12 per cent.; large mononuclears, 4 per cent.; transitionals, 1.33 per cent.; eosinophiles, 0.67 per cent.

The total twenty-four hours' urine of three days was examined during the preliminary control period, but not until four days had elapsed after the first short *x*-ray exposure, so that the results would not be influenced thereby.

x-ray exposures were begun July 4, and continued daily except Sunday until August 1, making twenty-six applications in all. She then returned home for a few weeks. The exposures were made over the neck and thorax in front, the rest of the body being protected, and a wet leather filter was used over the exposed area. The average duration was about fourteen minutes from a medium tube of two to three inches' spark resistance, with the anode ten to twelve inches from the skin. A mechanical spring interrupter was employed and a secondary current of 1½ to 2 milliampères used. There was a marked erythema at the time we stopped the treatments, but this disappeared in two or three weeks. There was a decided and progressive improvement in every respect from the beginning of the treatment. After a very few exposures she was able to sleep in a recumbent posture and on either side, and when she returned home she had no dyspnœa, even when going up stairs. The blood count made July 8, the day she left the hospital, showed: red cells, 4,240,000; leukocytes, 6560; hemoglobin, 62 per cent.; polymorphonuclears, 81 per cent.; lymphocytes, 6 per cent.; large mononuclears, 6 per cent.; transitionals, 6 per cent.; eosinpohiles, 1 per cent.

The portion of the growth in the neck had diminished in size and was softer. Dulness was not so pronounced in the regions of the apices and the breath sounds were more nearly normal. By comparison of the skiagraph made a few days after beginning treatment with the one made after the last exposure, we find some reduction in the side of the intrathoracic portion of the growth, amounting to about three-eighths of an inch in the width of the shadow. Along with this rather slight but encouraging decrease in size, there must have been considerable reduction in density to account for the marked improvement in pressure symptoms. While she was under observation there was no elevation in temperature. The respirations were slightly increased (20 to 24) and the pulse was accelerated at first, averaging about 100, but later came down to normal.

In the metabolism investigations the total output of nitrogen, uric acid, chlorides, and P_2O_5 was estimated. For the first twenty-four hours after treatment was started the waste tissue products showed, with the exception of the nitrogen, a *decrease* below the average of the preliminary control period, but on the second day there was a recovery, and the *average* for the *first four days* of treatment showed an increase in P_2O_5 and nitrogen and a decrease in uric acid and chlorides. The patient was discharged from the hospital July 8 after these investigations were finished, and readmitted July 24 and again placed on the special diet and the waste products estimated for three days, July 27 to 29. The average percentage of increase or decrease over the preliminary control period is shown in the accompanying table:

	P_2O_5		Uric Acid.		Nitrogen.		Chlorides.	
	Inc.	Dec.	Inc.	Dec.	Inc.	Dec.	Inc.	Dec.
	Per cent.		Per cent.		Per cent.		Per cent.	
First day of treatment .		19.87		23.67	13.74			16.23
First 4 days of treatment .	6.34			7.97	20.47			0.85
21, 22 and 23d days. . .	6.70			22.12	13.66		10.08	
2d leukemia case, 1905 .	200.00		60.00		70.00			

At the present time (November 15) this patient is still under treatment. She has been home twice, remaining several weeks each time, against our advice, and her condition is practically the same in every way as at the time of the above report.

By comparison of these results with those of the investigations in leukemia reported last year, we find a decided contrast. In the typical case of pseudoleukemia there is no evidence of an excessive tissue destruction neither during the first few days of *x*-ray treatment, nor during the third week, by which time there had been a recognizable decrease in the size of the large mass. Moreover, what little increase there was in elimination did not appear at once as in the second leukemia case. In our Hodgkin's case the increase in elimination of waste tissue products is no more than we would expect to find during the slow destruction of any other variety of growth of like size responding to *x*-ray treatment, but the increase *manifested itself earlier*. The results in pseudoleukemia differ on the one hand from those in leukemia, in which the treatment not only causes a reduction in the size of an enormous splenic tumor but also we are presumably stimulating an autolytic process which may or may not cause the reduction of the splenic mass, but at least institutes an *almost immediate* destruction of enormous numbers of leukocytes circulating in the blood. In contrast with a carcinoma on the other hand, the evidences of tissue destruction are manifest much earlier in pseudoleukemia, and the results of the experimental investigations of Heineke and of Warthin explain the reason.

The researches of Heineke[91] were undoubtedly the most valuable investigation in *x*-ray pathology up to the time of his report, and form the basis for our present knowledge of the action of the *x*-rays upon lymphatic structures. He found that the exposure of guinea-pigs for several hours

to the rays almost invariably resulted in death and the white cells of the bone-marrow and all lymphoid structures were destroyed, and the process was analogous in all these tissues. In the bone-marrow, for instance, the process started at nearly the third hour, reached its height at about the eleventh hour, and terminated by the end of the fifth or sixth day. He determined that in a rabbit or moderate sized dog the minimum exposure necessary to institute any degenerative changes was fifteen minutes. The lymphocytes were always the first to react. All these changes occur without any reaction of note in the skin. The reaction of the lymphoid tissue of man is not so prompt nor so decided. He deduces the important conclusion that when tumors of lymphatic origin regenerate or recur elsewhere, after an apparent disappearance or destruction, and *x*-ray treatment is suspended, it shows that although the principal manifestation of the disease has been eliminated, the treatment has not reached nor removed the cause. This statement has an important application in the treatment of leukemia and pseudoleukemia, in which relapses, following apparent cures are so very common.

About the same time, but independently of Heineke Warthin[92] made similar researches and obtained practically the same results. He observed changes in the lymphocytes in the spleen within fourteen minutes after an exposure of half an hour and found that disintegration continued for several days. As in Heineke's experiments, exposures of five hours or more caused death usually in from two to five days, and always before the eleventh day. He found that white rats were especially susceptible. The action upon lymphatic glands was similar, and repeated short exposures caused ultimate necrosis, but it was possible for regeneration to take place if the applications were discontinued. The reaction of bone-marrow was much less marked, and single short exposures produced no perceptible changes.

It is evident, therefore, that the lymphatic structures are not only the most susceptible of any tissues in their reaction to *x*-rays, so far as we know, but also destructive changes may begin almost immediately after exposures. The sudden and remarkable increase in elimination of waste tissue products in leukemic patients so treated can be explained by the autolytic action upon the leukocytes of the blood, but whether the destruction takes place in the lymphatic structures alone, especially the spleen and bone-marrow, or also in the blood, cannot be said to have been definitely proved. The researches of Smith and Capps[93] would tend to prove that the blood did, under such circumstances, contain an autolytic agent. In pseudoleukemia the exact cause of destruction is more difficult to determine. If it were dependent upon autolysis alone, as is the cause of lymphoid degeneration assumed from Heineke's experiments, it would be expected that there should be a marked decrease even below normal of the leukocytes in the blood of a patient treated for generalized lymphatic enlargements in pseudoleukemia, but such is not the case.

A third case of supposed Hodgkin's disease was treated this year and metabolism investigations made in connection therewith.

Case VII.—T. C. D., male, aged forty-five years. He presented marked enlargements of the glands on each side of the neck, causing great pain and considerable dyspnœa, and showing a tendency to soften. There was also an enlarged epitrochlear gland in the left elbow. The patient was very weak and emaciated and the blood examination showed a symptomatic anemia. *x*-ray treatment was started May 14, 1906, and he was given four daily exposures of eight to ten minutes each to the neck and one exposure over the spleen. After this his general condition and the pressure symptoms demanded more radical procedures and most of the enlarged cervical glands were excised. The pathologist reported the condition to be tuberculous adenitis. The case is of interest only because the metabolism investigations showed practically no change in the elimination of waste products under *x*-ray treatment.

In reviewing the literature on pseudoleukemia, references have been found for forty cases in which *x*-ray treatment was employed. This number must represent almost all the reports up to September 1, 1906. In reply to letters sent out for the purpose of obtaining the subsequent history and final outcome of cases previously reported, some writers have mentioned a few additional ones, and these will be included in the summary. As was previously stated in connection with leukemia the reports probably do not include more than half the cases that have been treated and for the same reasons.

Summary.

Cases reported in literature	40
Cases fully reported by letter	4
Total	44

In all but two of these cases, the primary results obtained by the treatment have been found, and are as follows:

Symptomatically cured	18
Improved	14
Not affected, or improved but slightly	10

Of the 44 cases included in the table, final reports have been received or found of 29, or 66 per cent. Three patients are known to have disappeared during or after treatment, and the authors have no knowledge as to their subsequent histories or whereabouts. Final reports of the remaining 12 cases could not conveniently be obtained at present.

Out of the 29 cases in which the final outcome or present condition are known, 7 are still alive and well three

to four years after the first symptomatic cure, and 1, one year afterward. Seventeen have died of the disease actually, or as a result of it, and 2 more will probably die soon. The remaining 2 cases are still under treatment. At least four of the patients died during relapses, and four of those still living have had relapses.

In conclusion, out of 29 cases reported fully to date (or 66 per cent. of the total number) 24.1 per cent. are alive and well three to four years after the first symptomatic cure, and altogether 27.6 per cent. are alive and well; 65.5 per cent. are dead or will soon die; and 6.9 per cent. are still under treatment.

Dr. E. G. Williams has advised me of one unreported case now under treatment and almost symptomatically cured, and Dr. J. G. Williams, of one in which the progress is very favorable.

It may be of interest to note that at least three cases have died as a result of a toxemia induced by the treatment, two have died of peritonitis, probably due to intestinal perforation, one of pulmonary tuberculosis (which may perhaps be questioned), and one of inspiration pneumonia, following an operation upon the glands in the neck. In one case, which was symptomatically cured in 1903, and is still well, without having had a relapse, toxic symptoms were noted during the entire time of treatment. In this case all the superficial glands and those of the mediastinum were known to be involved, and the patient was decidedly anemic.

The results of the *x*-ray treatment of pseudoleukemia are not as encouraging, I think, as most of us had believed, but they are certainly very much better than in leukemia. In view of the rather high death-rate, the frequency of relapse, and the results of experimental research, the *x*-ray can hardly be termed a specific therapeutic agent in this disease. However, it undoubtedly has a marked influence upon the disease and the general condition of the patient usually improves to such an extent that a symptomatic cure may often be obtained. But it is questionable if the *x*-ray treatment alone removes the cause. If the patient remains well, the treatment may have brought about such a favorable state of affairs that the etiological factor disappears through some other agency. There is, however, more ground for believing that the rays really do, of themselves, eradicate the disease than in leukemia.

The points in favor of the *x*-ray treatment of pseudoleukemia are:

1. A cure for at least three or four years may be obtained in something like 25 per cent. of the cases treated.

2. In almost all cases not so cured, life is prolonged during a period of comparative comfort by improvement in the general condition or by the relief of pressure.

3. No other therapeutic agent can yield results as good.

4. By further improvements in technique and a better understanding of the pathology of the disease, even more favorable results are possible than are obtained at present.

The first report of a case of pseudoleukemia treated by the *x*-ray was made by Pusey[6] in January, 1902. Later in the same year, Stover, Hett, Dunn, and Childs reported other cases. From then on the references in literature are numerous and frequent.

POLYCYTHEMIA.

The literature concerning any form of treatment of this condition is scarce, and I have found records of four cases only treated by the *x*-ray. There have been undoubtedly numerous other cases so treated and not reported because of the failure to accomplish any good results. The administration of arsenic and splenectomy seem to be the methods more generally employed, while deprivation of iron, venesection, and radiotherapy[98] are among the other measures that have been tried. The results cannot in any case be said to be very favorable. Turk reports 7 cases with enlarged spleen, in only 1 of which was there any improvement. This patient was treated with arsenic, which was administered with the idea that it checks the proliferation of the blood-forming tissues, as in splenomedullary leukemia. In one of Heineke's[95] early reports of his experiments, he states that after prolonged exposures there were evidences in the spleen of a destructive action of the rays upon the red corpuscles.

In the absence of more definite knowledge it would seem that the splenic area, at least, is the proper place for *x*-ray exposures in patients so treated. Pfahler[96] last year reported 1 case under *x*-ray treatment with improvement while continuing the exposures. Eichberg[97] states that Joachim and Kurjuwet have reported 2 cases so treated, and last year I made a preliminary report of 1 case under my care.[28] As a detailed report of this case will probably be published later, I shall mention simply the further progress under *x*-ray treatment:

Case VIII.—W. B., male, aged twenty-two years. Referred by Dr. Stengel, May 13, 1905. Red cells 10,000,000, marked cyanosis, slight dyspnœa, general weakness, slight enlargement of the spleen. Fifty exposures of five to ten minutes each were made over the splenic area from May 13 to September 24, 1905, after which the preliminary report was made. A hard tube was used with the anode about twelve inches from the skin. Up to that time his general condition was improved, he felt stronger, and the blood count varied from 8,000,000 to 9,500,000. From September 24, 1905, to the present time he has received seventy additional exposures, averaging two per week, regularly, until July 21.

SYNOPSIS OF REPORTED CASES TREATED BY THE X-RAYS.

Pseudoleukemia.

Number.	Author.	Reference number.	Probable duration of disease.	Effect of X-ray upon			Result.	Relapse.	Final outcome or present condition.
				Spleen.	Glands.	Relapse.			
1	Pusey	6 to 8	....	Not enlarged	Reduced to nearly normal	1st, cured; 2d, no effect	Almost symptomatic cure	1st in 3 months; 2d in 1 month	Died—inspiration pneumonia
2	"	"	....	....	Entirely disappeared	1st, cured; 2d, cured in 1 month; 3d, cured, 1904	Symptomatic cure, 1902	1st in 8 months; 2d in 2 years—mediastinum; 3d in neck and groin	Still well, Aug., 1906*
3	"	15	....	.. .	No effect (last stages of cachexia)	....	No effect	....	Died
4	"	"	....	....	Entirely disappeared after 9 exposures	Cured	Symptomatic cure, July, 1902	Slight relapse, 1904	Still well Aug., 1906*
5	Stover	1	....	....	All disappeared except one, which was excised later	Cured	Almost symptomatic cure, 1902	Relapse in new area; cured	Still well, Sept., 1906*
6	"	2	About 2 or 3 years	. ..	No effect; glands excised and recurred	....	No result under x-ray	Relapse after excision	Nothing known of patient*
7	"	"	18 months	....	Decidedly reduced at first, later no effect	....	Slight improvement; stopped treatment	....	Patient disappeared*
8	"	"	....	....	Decidedly reduced	....	Improved; stopped treatment	....	Patient disappeared*
9	"	"	....	....	Enormous glands disappeared after 12 exposures	....	Symptomatic cure	....	Died probably intestinal deposits caused perforations
10	Hett	5	....	Slightly enlarged	Reduced to nearly normal	....	" "	Died 9 months later tuberculosis	Died*
11	Dunn	4	....	....	" " " (neck)	....	" " 1903	None	Died later of pulmonary tuberculosis*
12	Childs	3	....	Slightly enlarged, reduced to normal	Enormous glands reduced to nearly normal	. ..	Still under treatment at time of report. Later cured, 1903	None	Living and well, Sept., 1906*
13	Steinwand	9	....	Moderately enlarged	Almost entirely disappeared	....	Symptomatic cure, 1904		
14	Finch	10	2 years	Slightly enlarged (marked anemia)	All superficial glands and large mediastinal mass	1st, cured; 2d, not responding (Sept., 1905)	" " "	1st in 4 months; 2d in 1 year	Condition very grave, Aug., 1906; will die*
15	Lommel	11	....	....	....	....	Improved	....	Died during treatment
16	Krause	12 & 13	....	....	....	....	Symptomatic cure, Dec., 1905		
17	"	"	....	....	....	....	No benefit	....	Died
18	Levy-Dorn	14	....	....	....	....	Symptomatic cure, Dec., 1904		
19	Holding and Warren	16	14 months	Not enlarged	All superficial glands and those of mediastinum	1st cured; 2d not treated	Much improved; stopped treatment, 1905	1st in 3 weeks; 2d not treated	Died, 1905*
20	Williams, F. H.	17	1 year	....	....	No effect	Symptomatic cure	Relapse in 7 months	Died
21	"	"	....	....	....	....	Improved, but stopped treatment		
22	"	"	....	....	....	....	Treatment just started, 1903		
23	Coley	18	....	....	....	....	Much improved		
24	Allen	"	....	....	Glands somewhat reduced	....	Improved		
25	"	"	Over 1 year	....	Glands of neck and axillæ. No effect yet. (Pronounced anemia)	....	No improvement; still under treatment		
26	Hulst	19	....	....	....	....	Much improved by 12 applications	....	Died 2 days later
27	Stokes	20	....	Slightly enlarged	Deep pelvic and superficial glands; entirely disappeared	Cured	Symptomatic cure, May, 1905	Slight relapse in 9 mo.	Still well, July, 1906*
28	Williams, J. G.	21	2 years	....	Deep and superficial glands greatly reduced by 5 applications	....	Severe intoxication (cough and edema of legs)	....	Died during treatment—toxemia*
29	Butler	22	9 months	Not enlarged, but somewhat painful	Both sides of neck. (Dyscrasia)	....	Improving at time of report, 1902	....	Final reports obtainable later*
30	"	"	....	....	Slightly reduced	....	Improved but stopped treatment and disappeared	....	Final reports obtainable later*
31	"	"	....	....	....	....	....	....	Final reports obtainable later*
32	"	"	....	....	....	....	....	....	Final reports obtainable later*
33	Pfahler and Shoemaker	23	....	Enlarged; decreased to nearly normal	Axillary, inguinal, retroperitoneal, and mediastinal. Reduced to ⅓ size	....	Not improved by 6 exposures	....	Died in 10 days.
34	Senn	24	1 year	Considerably enlarged (marked anemia)	Mediastinal and all superficial. Entirely disappeared	Toxic symptoms during entire time of treatment	Symptomatic cure, 1903	....	Still well Aug., 1906*
35	Stoll	25	5 years	Slightly enlarged (anemia)	Superficial (cervical and axillary) almost disappeared; mediastinal and pelvic not affected	....	Only slightly improved	....	Died—peritonitis
36	Rosenberger	26	5 years	....	....	....	Not improved	....	Died in 2 months
37	Hunter	27	....	....	....	....	Improved; still under treatment, March, 1906	....	Still under treatment

38 Pancoast	28	6 months	Slightly enlarged; feels Only superficial glands	...	Improved for a while but	...	Probably died
"			enlarged and more numerous; enlarged considerably		stopped treatment		
39 "	"	8 months	again at intervals	reduced			
			Not enlarged	Only mediastinal glands	Improving; still under		Still under treatment
				enlarged; mass is decreasing in size	treatment, Nov., 1906		
40 Childs	105		Enormous superficial glands, considerably reduced	....	Improved		Died while under treatment
41 Williams, J. G.	L		....	....	Symptomatic cure		Died suddenly in 1 month*
42 "	L		....	....	Not improved		Died during treatment*
43 Dana	L		Enlarged glands of neck None		Symptomatic cure in 9 months	None	Still well, Aug., 1906 (3 years)*
44 "	L		Cervical glands, subsided None considerably during treatment; mediastinal mass reduced the same ever since	....	Treated 1 month and stopped. Appears to have been a malignant case, though unexpected, 1903		Still well, Jan., 1906 (3 years)*

* Final reports of cases received by letter from the authors of the original reports.

L Cases not reported in literature, but data received by letter. (Cases 41 to 44.)

The count was as low as 7,110,000 in May and the patient then felt fairly well but was still weak. When last seen, August 4, he was in about the same condition as when first treated, and the question of splenectomy was being discussed. He has never had any other form of treatment than the *x*-ray and has been working continuously while under our care. The accompanying table shows the blood counts since the last report:

September 16, 1905, 7,950,000; 30th, 6,800,000.

October 7th, 8,200,000; 21st, 8,250,000.

November 18th, 7,600,000; 27th, 8,200,000.

January 6, 1906, 9,220,000; 13th, 8,800,000; 22d, 8,800,000.

February 3d, 8,800,000; 10th, 10,000,000; 24th, 9,240,000.

March 3d, 8,800,000; 10th, 8,500,000; 17th, 8,240,000; 24th, 8,160,000.

April 7th, 9,030,000; 28th, 7,720,000.

May 12th, 7,110,000.

June 2, 8,390,000; 9th, 7,420,000; 23d, 9,430,000 (white blood corpuscles, 10,320; hemoglobin, 135 per cent.); 30th, 9,080,000.

July 7th, 7,960,000; 14th, 8,725,000; 21st, 8,920,000.

August 4th, 10,020,000.

SPLENIC ANEMIA.

In going over the literature on the other conditions included in this paper, I have collected reports of 12 cases of splenic anemia treated by the *x*-ray. Bozzolo[99] has treated 3 cases with some improvement, though the reaction has been slow. Pulley[100] reports 2 cases improved. Schirmer[101] refers to 4 cases improved. Krause[79] treated 3 cases, with improvement of the blood condition, but the spleen was not reduced in size.

PERNICIOUS ANEMIA.

So far as I know 5 cases of pernicious anemia have been treated by the *x*-ray. Renon and Tixier[102] report 1 case in which the *x*-ray was used in conjunction with diphtheria antitoxin. The disease was of eighteen months' duration and the patient a woman sixty-eight years of age. After three months of combined treatment the red cells rose from 880,000 to 2,405,000 and the leukocytes from 2000 to 4000, and her general health was considerably improved. As the reaction to each agent was found to decrease gradually as treatment progressed, they were used alternately with better results. The substance of their theoretical grounds was that the bone-marrow was stimulated by leukolysins due to *x*-ray destruction of leukocytes and by hemolysins formed by the action of the antitoxin.

Last year I referred to 2 cases treated at another hospital in Philadelphia. In 1 there was rapid and marked improvement under *x*-ray applications, followed by a relapse one year later, but again responding rapidly to the same treatment. This patient is probably still alive. The second

patient who showed evidences of an intoxication received one exposure of eight minutes over the thighs, and this was followed in a few hours by alarming symptoms terminating in death in two and one-half weeks. At this same hospital, strange to say, a third case has been treated lately and when last heard from the patient was improving.

In November, 1905, I was asked to try the effect of the rays on a case of pernicious anemia referred by Dr. Stengel. Realizing the dangers of such a procedure the exposures were to be exceedingly short, and Dr. Edsall had the case under observation for the effect upon metabolism. The patient, a male, aged thirty-eight years, had a blood count near 1,000,000 red cells, some elevation of temperature, an irritable stomach, and was considerably prostrated. The elimination of waste tissue products during a preliminary control period gave evidence of toxic tissue destruction. On November 11 I gave him one exposure lasting only four minutes, over the abdomen, using a hard tube of four inches' spark resistance, with the anode twelve inches from the skin. A mechanical spring interrupter was used and the secondary current was 1 milliampère. Three or four hours later he had a chill and vomited, the temperature rose to 103°, and for several hours he was alarmingly ill. During the first twenty-four hours the elimination of tissue products was reduced about 50 per cent., and during the second twenty-four hours, while he was recovering, the nitrogen and P_2O_5 rose markedly, but did not reach the average point of the preliminary control period until the third day. The uric acid did not recover for four or five days. The patient died three weeks after the single exposure.

These facts are worthy of serious consideration. While not believing that *x*-ray exposures are absolutely contraindicated in pernicious anemia I shall hereafter be emphatic in my refusal to treat, or even skiagraph, except for urgent necessity, such a patient, unless metabolism investigations are carried out in conjunction, and the individual does not show evidences of a toxemia and does not react to other forms of treatment. It is not always possible to study the metabolism in our patients, and in fact for many of us it will be impossible; but Dr. Edsall thinks that as a rule the estimation of the uric acid accompanied by a careful simple urine analysis will answer, and this is the easiest and quickest determination of all the products.

In connection with this subject it may be well to mention some facts concerning another of Dr. Edsall's cases. A patient with rheumatoid arthritis was given a few minutes' exposure to the elbow, the remainder of the body not being protected. The subsequent clinical phenomena and the results of the metabolism investigations were exactly similar to those in the case just mentioned and even more striking in some respects. These experiences should be sufficient to teach us a lesson in caution. In addition, by "reading between the lines" while reviewing the literature on leukemia and pseudoleukemia, I have found several instances in which rather sudden death has resulted from evidently indiscreet *x*-ray exposures. You may be assured that there is sufficient evidence at hand to warn us not to expose to *x*-rays, either for therapeutic or skiagraphic or fluoroscopic purposes, patients suffering from grave diseases, especially when there are evidences of severe toxemias. In this category I would place such conditions as pernicious anemia, pneumonia, typhoid fever, acute nephritis, pyemia, and under certain circumstances even leukemia and pseudoleukemia.

Certainly, the rays should not be used for experimental purposes in such cases.

It is possible to recall one instance of a short skiagraphic exposure markedly influencing metabolism. In January, 1906, Dr. Edsall referred a case of unresolved pneumonia of the left base for applications of *x*-rays, with the view of hastening, by means of the stimulation of autolysis, a resolution which had been at a standstill for two weeks, and also to study the metabolism, as had been done with several other cases. Before beginning the treatment I desired to make a skiagraph of the chest for comparison and deferred the therapeutic application until the next day. Although this skiagraphic exposure lasted but eight seconds, the effect upon metabolism was remarkable. The output of nitrogen rose over 100 per cent. during the following twenty-four hours and the chlorides increased about 60 per cent. After this, mild exposures of five minutes were given daily, and as resolution progressed the elimination gradually subsided to the normal point of the control period on the eighth day when all abnormal physical signs had disappeared.

In concluding these remarks concerning some of the dangers attending *x*-ray applications, let us realize that for our own reputations and protection we have the right to demand a satisfactory report from the clinician referring the patient to us, and for the same reasons, applied to himself, he should be careful and willing to give one. No more than this is required by the surgeon before he orders the anesthetic to be administered to his patient. Dr. Edsall has given this advice to the clinician, and I take the liberty of putting it in proper form to be received by the *x*-ray specialist.

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PRIMARY SQUAMOUS CARCINOMA OF THE GALL-BLADDER.

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Recent studies demonstrating the transformation of one type of tissue to another, or even the metaplasia of one type of cell to that of a different variety, are of sufficient importance to warrant the report of a single case, and any conclusions which may be drawn from a study of the collected cases of that type.

The patient, whose history follows, was transfered by Dr. Alfred Stengel to the surgical service of Dr. Charles H. Frazier, to both of whom I am indebted for permission to report the case.

The patient, a widow, aged sixty-nine years, gave the history of pain in the lower part of the left chest, of eight months' duration, and gradually becoming more severe, at times radiating to the back. The pain was attributed to an injury, the traumatism being apparently confined to the left side. She never had any jaundice, vomiting, nausea, or abdominal pain. Previous history and family history are unimportant. On examination a slightly movable, tender mass was palpable, extending from the costal margin to the umbilicus on the right side. Because of several attacks of abdominal pain while in the hospital, and the development of jaundice and vomiting, an operation was determined upon and the abdomen opened. The gall-bladder was found enlarged, adherent to the surrounding tissues, which were separated, the cystic duct ligated, and the organ extirpated. During its removal the walls were ruptured and a considerable amount of pus, necrotic tissue, and gallstones escaped. The patient made a good recovery from the ether, but died two days later in a delirious state. The autopsy showed a small area of carcinoma on the under surface of the liver, arising by direct extension from the gall-bladder, the liver being the seat of a biliary cirrhosis. There was no evidence of other primary or secondary growths in the body.

Description of the Gall-bladder. The gall-bladder is enlarged, the upper portion torn and irregular, from which opening a mass of tissue, thick pus, and calculi escape. The external surface contains numerous fibrous adhesions and the bloodvessels show engorgement. On opening the gall-bladder the mucous membrane at the fundus shows numerous ulcerated areas, and in a few places is infiltrated by a friable, fungous mass, white in color, and distinctly papillomatous in character, in which the calculi (forty-five) are embedded. The tumor infiltrates the wall of the organ, which measures from 1 mm. to 2 cm. in thickness, and in one area shows a thickening of the peritoneum to which the tumor has extended. The portion of the cystic duct attached to the bladder is free from change.

Sections for microscopic study were taken from the ulcerated mass at the base and from the fundus of the gall-bladder. In the former sections the mucosa was absent; in such areas a hemorrhagic and cellular exudation is present, the bloodvessels being considerably engorged. The connective tissue is thickened and hyaline in appearance, apparently as the result of a long-continued irritation. Toward the underlying parts the carcinomatous infiltration begins, and occurs as elongated, finger-like processes. The cells on the outer part of these projections are cuboidal in shape, but toward the centre become flat and form numerous pearly bodies, many of which are of exceptionally large size, but do not show the same characteristic concentric arrangement of skin cancers. Prickle cells are quite abundant, while in the stroma apparently as a cellular reaction, are many eosinophilic leukocytes. The tissue studied from the fundus of the organ likewise shows an ulceration and atrophy of the mucosa. In some areas, however, there is a distinct lining composed of from five to eight layers of cells. Those situated

next to the bladder wall are cuboidal in shape with deeply staining nuclei; those in the central layer are more compressed, while the superficial cells are decidedly flat and horny, the nuclei barely perceptible or absent. These cells likewise show the processes of prickle cells, but to a less extent than the growth at the base. The wall of the bladder is also involved in a cancerous process; it is not possible, though, to trace this malignant change to the metaplastic epithelium.

The diagnosis of squamous carcinoma of the gall-bladder cannot be doubted from the above findings, and especially in view of the fact that metaplasia was discovered in the mucosa, although that membrane was ulcerated for the

Fig. 1.—Photograph of the gall-bladder, showing calculi and the tumor mass.

greater part. The presence of metaplasia was also demonstrated in the cases of Deetz and Weber.

In explaining the origin of a squamous-cell carcinoma of the gall-bladder we must accept one of two views: a direct metaplasia of the normal columnar cell lining into squamous epithelium, or the development of the tumor from embryologically misplaced epithelium. Many authors have endeavored, by the latter theory, to explain these growths, but they lose sight of the fact that in its development the gall-bladder is brought in no way into association with the derivatives of the ectodermal layer. For this reason, alone, the question of a misplaced anlage as a causative factor is excluded. Ribbert believes that a true metaplasia occurs only in areas which lie near ectodermal tissues, and that one can, without difficulty, trace the position of the abnormally situated anlage, or in other instances the extension from the ectodermal parts can be followed directly to the new growth. While this may occur in certain regions, as, for example, in squamous carcinoma of the uterine body, yet it is impossible to have such an extension in other organs. Lewisohn observes that this view cannot be held in the case of squamous carcinoma of the pancreas which he describes, and in the same way it cannot be applied to the gall-bladder.

As to a consideration of metaplasia in general, it may be defined as a transformation or substitution of specific cells or tissues by a structure also specifically differentiated and arising from the same tissue (Lubarsch). The conception of metaplasia is to be sharply defined from anaplasia (Hanse-

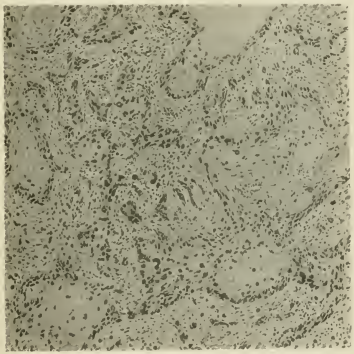

Fig. 2.—Photomicrograph of the gall-bladder wall containing pearly bodies and prickle cells.

man) and still more so from pseudometaplasia. The latter term is applied to cells flattened by pressure, as in cyst formation in glandular structures, but in no way do these flat and compressed cells resemble in minute structure the metaplastic results in the case of a transformation of cylindrical epithelium into squamous cells.

In reviewing the literature of metaplasia, one is struck with the large number of reported cases, and particularly in the variety of organs in which this change has occurred. Briefly, well-marked and carefully studied cases have been observed in the mucosa of the nose, the ear, a great part of both the respiratory and alimentary tracts, the gall-bladder, the urinary system, uterus, and urethra. Besides these clinical data, the transformation has been experimentally produced by Lubarsch, who induced the change in the bladder

mucosa of rabbits. A defect was first made, followed by chemical irritation, in order to retard healing; gallstones and cherry-stones were then inserted, from the irritation of which island-like areas of metaplasia resulted. Fütterer, after extensive experiments on the stomachs of rabbits, was able to demonstrate this change in four instances, and conclusively traced the transformation of glandular epithelium into squamous cells.

Two forms of metaplasia are distinguished by Lubarsch. In the first, or regressive type, the old or original cells lose their former peculiarities and assume others of inferior nature. In the second, or progressive form, the metaplasia is associated with cell proliferation; the old cells do not change, but after their destruction the new ones, under changed conditions, assume the characteristics of a new and distinct type, and not the distinguishing features of the mother cells. The majority of cases have been observed to belong to this class.

As the exciting cause in the production of metaplasia

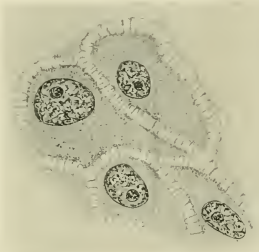

Fig. 3.—Prickle cells found in the carcinomatous areas.

great emphasis is rightly placed upon prolonged mechanical irritation. Thus, the chronic catarrh of the nose and the air passages, calculi in the gall-bladder or kidney, lead at times to the production of metaplasia, which, in turn, assumes importance because of its tendency to undergo malignant degeneration. Metaplasia of entodermal epithelium, as, for example, the entodermal lining of the gall-bladder, into squamous epithelium, is rare, but this form is exceedingly malignant. In respect to the gall-bladder, metaplasia is relatively uncommon; Deetz was not able to find such a change in 300 bladders removed for cholelithiasis. That it constitutes a grave pathological lesion is shown by the cases recorded, in which the percentage of deaths was very high (93 per cent.). It must not be assumed that simple mechanical irritation acts alone as the cause of metaplasia, but if that condition is continuous, and in addition there is a resulting circulatory disturbance, Futterer thinks a metaplasia is likely to result. The importance of this mechanical action as the cause of metaplasia, and especially that form which leads most readily to cancer formation or to the variety of carcinoma without metaplasia, should receive very careful consideration.

Upon the above grounds, then, it is the belief of the author that the case reported is of metaplastic origin. As already pointed out, tumors of this type are apt to be very malignant. Death resulted in all the cases noted from the effects of the carcinoma. (Bevan's case is not fully recorded.) In the present case—and the same fact was observed in other instances—the disease was slow and of insidious nature, producing few early symptoms referable to the gall-bladder. Biliary calculi were mentioned as being present in fourteen of the fifteen recorded cases, a percentage higher than their occurrence in the ordinary forms of cancer. While the

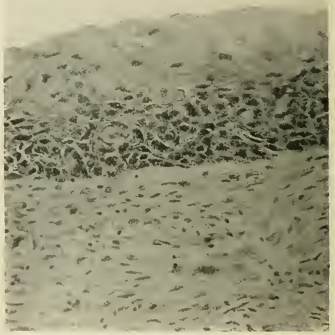

Fig. 4.—Photomicrograph of the mucous membrane, showing metaplasia.

treatment of this variety of cancer does not differ from that of the usual form of gall-bladder carcinoma, yet the fact that the presence of stones or a catarrh may lead to metaplasia, and this, in turn, to a very malignant degeneration, should act as still another reason for early operative interference in gall-bladder disease while the process is still in the benign stage.

List of Cases of Primary Squamous Carcinoma of the Gall-Bladder.

Case I (Ohloff).—The patient, male, aged sixty-nine years, died with the symptoms of a carcinoma of the liver. The autopsy revealed a tumor occupying the gall-bladder,

measuring 8 x 6 cm. and extending to the liver tissue. The wall of the bladder was thick, rigid; the mucosa smooth; the lumen contained six stones. Small metastatic nodes were found in the liver.

Microscopically, the tumor was composed of squamous, epithelial cells, and contained pearly bodies; the metastases showed the same characteristics as the primary growth.

Case II (Ohloff).—Woman, aged sixty-five years; did not have anything in history of importance. At the autopsy a tumor of the gall-bladder was found; extension to the liver and duodenum had arisen. Twenty calculi were found in the bladder. Diagnosis: Squamous carcinoma.

Case III (Zenker).—This author reports the autopsy on a woman aged sixty-seven years, in whom a tumor of the gall-bladder was found; metastases to the liver; gallstones present in bladder.

Microscopically, the growth was composed of cylindrical and squamous cells, with no evidence of hornification in the latter.

Case IV (Pollock).—Female, aged sixty-four years. The autopsy showed a tumor of the gall-bladder and calculi; secondary growths in the liver and lungs. The greater portion of the bladder was transformed into a soft, pulpy mass, the entire wall being involved. The mucous membrane, on microscopic examination, contained a few glands lined with cylindrical epithelium. The cells elsewhere resembled in their arrangement the epidermis, prickle cells being present. The metastatic tumors contained prickle cells and pearly bodies.

Case V (Pollock).—Female, aged sixty-five years. At the postmortem examination the gall-bladder contained a tumor mass and biliary calculi. Metastasis to the liver, duodenum; retroperitoneal and retrotracheal nodes; perforation of gall-bladder and peritonitis. Microscopic diagnosis: Squamous-cell carcinoma, prickle cells present.

Case VII (Nehrkorn).—The patient, female, aged sixty years, had been ill for nine months with pain in the liver region, jaundice, no colic; death. There was found an infiltration of the gall-bladder wall, twelve stones, metastases to the portal nodes, liver, and duodenum. The mucosa was atrophied in microscopic sections, but the wall contained a squamous carcinoma, pearly bodies being present only in the lymph-node metastasis.

Case VIII (Deetz).—Female, aged fifty-four years. Exploratory laparotomy for symptoms of carcinoma of the gall-bladder, at which extensive metastasis was found. Autopsy: Tumor of bladder with extension to liver, peritoneum, and lymph nodes; gallstones present. The mucous membrane for the greater part was destroyed; in one small area the membrane was present and here was arranged in layers. Diagnosis: Squamous carcinoma containing prickle cells and pearly bodies.

Case IX (Deetz).—Woman, aged forty-nine years, died with symptoms of carcinoma of the gall-bladder. The autopsy disclosed an extension of a gall-bladder tumor to the liver, gallstones, metastatic nodes in the liver.

Pathological changes in the mucous membrane could not be demonstrated; the tumor infiltrated the wall and contained pearls, but no prickle cells.

Case X (Deetz).—Neoplasm was adherent to the colon; the bladder contained stones. Microscopically, there was present a squamous-cell growth containing pearls and prickle cells. In this case there was also associated an adenocarcinoma which originated in the common duct, but had no connection with the epithelioma.

Case XI (Deetz).—Female. Autopsy report: Stones in gall-bladder, metastasis to liver. The mucosa destroyed, the underlying tissue being infiltrated with squamous and cylindrical cells, pearly bodies and prickle cells being demonstrated. There was an associated, malignant growth of the rectum in this case, a cylindrical-cell carcinoma.

Case XII (Bevan).—A man, aged fifty-five years, gave symptoms of cholelithiasis, with loss of weight. The bladder at operation contained pus and stones. Microscopic diagnosis: Adenocarcinoma and squamous carcinoma. Case has not been reported so far as known.

Case XIII (Zenker).—Woman, aged sixty-seven years. Metastases were found at postmortem in the lung, pleura, liver; gallstones in bladder. Microscopically, the tumor contained cylindrical and squamous epithelium, but no distinct horny layer was seen.

Case XIV.—Woman, aged sixty years; symptoms of cancer of the liver, with marked jaundice; no gallstone colic present. Autopsy: The gall-bladder showed in the upper portion an irregular, thickened wall with an ulcerated surface; forty stones. Microscopically, the epithelium where preserved was seen in several layers, the topmost cells being horny in character. The bladder wall likewise showed invasion of this misplaced squamous epithelium.

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Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson, Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

THE MAKING OF A MUSEUM OF APPLIED ANATOMY.

By Gwilym G. Davis, M.D., M.R.C.S. Eng.,
Associate Professor of Applied Anatomy, University of Pennsylvania.

In the teaching of applied anatomy the subjects discussed can usually be illustrated by preparations made from the cadaver. As to the desirability of well illustrating such a course by anatomical preparations there can be no question, but the extent to which this is carried depends not only on the ingenuity of the teacher, but especially on the facilities and time at his disposal.

One set of preparations is necessary for the use of the teacher in giving the demonstrations, but it is in the highest degree desirable that a duplicate collection be made, suitably mounted, and so displayed as to be freely accessible to the students, so that they can consult and study them at their leisure.

As museums of applied anatomy are as yet in an embryonic stage, it will only be by an exchange of individual experiences that we will be enabled to decide: first, what kind of preparations are desirable; second, how shall they be made, and third, how shall they be preserved. To those who have had experience in making museum preparations the task will be somewhat lightened, but many of those desiring these working museums will have had almost no such experience, and, to them, even elementary methods and procedures will be of benefit. While ordinary anatomical and pathological museums are to be found in all teaching institutions, I know of no museum in which the preparations have been made with the object of especially illustrating the application of anatomy to the explanation of the functions of the body in health and disease, of the causes and results of disease and injuries and their treatment.

What Kind of Preparations are Desirable? The preparations fall naturally into two classes: one illustrating the normal topography of a part, and the other the affections to which it is subject. Topographical anatomy is inseparable from applied anatomy, and the museum should contain as many specimens as possible illustrating it. The following will serve as suggestions:

The skull and brain can be readily illustrated. The triangles of the neck; anterior view of the structure of the neck; the organs of the thorax and abdomen; the axilla, bend of elbow, forearm, palm of hand, region of Scarpa's triangle, Hunter's canal, popliteal space, front and back of leg, dorsum of foot, sole of foot, arches of foot, etc.

In some cases other preparations will be of service, such as ligamentous preparations of the joints, to explain their action. Also muscular preparations to explain the construction of the limbs, etc. Special preparations illustrative and explanatory of the various affections should be made to an extent far greater than is as yet prevalent.

Skulls can be prepared illustrative of cerebral localization and showing the sites of operative procedures. The bones can be removed, showing the position of the arteries and venous sinuses. The membranes can be removed, showing the location of the fissures, etc. Brain preparations may be made, illustrating the effects of apoplexy, cerebral softening, the course of sight (as in the production of hemianopsia), and other brain lesions.

The mode of access to the various air sinuses, of reaching Meckel's and the Gasserian ganglions, catheterization of the Eustachian tubes, and rhinoscopy and laryngoscopy can be illustrated, also operations on the turbinated bones. In the neck, preparations may illustrate the ligations of arteries and operations on the air passages and thyroid gland; in the chest and abdomen it is mainly a question of topography, but it is instructive to dilate the lungs and pericardium. As yet the operations on the chest are comparatively few, but those on the abdomen are legion. Special preparations, illustrative of operations and mode of obtaining access to the bile passages, gastro-enterotomy, appendicitis, kidneys, and female genital organs, all can be illustrated. Hernia is another field. In the extremities, fractures and luxations can almost all be artificially produced, and preparations made illustrating their pathology and treatment. Amputations, ligations of arteries, resections, and palmar and plantar abscesses can all be illustrated; as well as other operations, such as the mode of access to the hip-joint and knee-joint, etc. As can be seen, the field is limitless and the above list is by no means intended to be complete.

How are the Preparations to be Made? In the making of preparations intended to illustrate the topography of a part, two methods may be employed. One consists in the dissection of a subject injected with a 10 per cent. solution of formaldehyde. This method is particularly valuable for preparations of the viscera, and may be combined with freezing when transverse sections are desired. Occasionally it is of service in the extremities, but the tissues are so hardened and bleached and the fibrous tissues and fasciæ are so

dense that the identification of individual structures is extremely difficult, and sometimes impossible. The other and more generally useful method consists in injecting with an ordinary non-hardening preserving fluid, and then making the desired dissection, taking care to disturb the normal relations of the structures as little as possible. On the completion of the dissection any structures which have been disturbed are to be carefully replaced in their previous position and the specimen immersed in a solution of formaldehyde, and there allowed to remain until the specimen is thoroughly hardened. After being set by the formaldehyde the specimen can then be either kept in a tank with some preservative fluid and used for demonstrations in teaching or preserved in a museum. The coloring of the arteries red, the veins blue, and the nerves yellow with ordinary water colors will add to the attractiveness of the specimen and enable the various structures to be more readily identified. In some cases pathological conditions can be utilized, such as empyema or pleurisy, illustrating displacements of the thoracic organs; also enlargements of the liver, stomach, hernias, hydrocele, etc.

To illustrate joint lesions the various joints can be injected with paraffin or wax tempered with tallow. This can best be done by immersing the joint deprived of its skin covering in a basin of hot water. The melted wax is then injected through an aspirating needle into the joint by means of a syringe. After the wax has hardened the part is dissected as desired. In this manner wax injections of all the joints can be made. In the same way the sheaths of the tendons of the flexors of the fingers and the extensors on the back of the wrist can be demonstrated, the wax being colored with vermilion or Prussian or ultramarine blue if desired.

To illustrate the effects of plantar and palmar abscesses colored wax can be injected beneath the fasciæ.

In making preparations illustrative of fractures it is usually better to first dissect and expose the parts to the extent desired and then make the fractures. In some cases, however, the fracture can be first made and then the dissection completed. In fracture preparations the muscles are the most important structures, as it is usually the influence which they exert in producing displacements that it is desired to illustrate and explain, and in such cases it is best to remove all other structures. The preparations desired for use in demonstrations should remain soft, and are to be kept in tanks with some antiseptic fluid which prevents the growth of molds, such as thymol or carbolic acid, to which a small amount of formaldehyde is to be added, as well as a small amount of glycerin. Too much formaldehyde will harden the specimens and is to be avoided. Glycerin tends to keep them pliable.

To be of service the fractures have to be made in certain definite directions. This is accomplished by first weakening the bone by perforating it with a drill or nicking it with a chisel and then completing the fracture by manual or instrumental force. By these means quite staisfactory preparations illustrative of fractures of the jaw, surgical neck of the humerus, clavicle, elbow, radius, femur, tibia, and fibula, etc., can be produced.

In the preparations of luxations these are practically all produced by hyperextension often assisted by a thrust or twist. The lower jaw is to be pried open as widely as possible, and if it cannot be luxated by pushing the condyle forward it may be accomplished by a blow with a mallet, a small block of wood intervening.

The shoulder can be luxated by having the body firmly bound, or held to the table, while the arm is hyperabducted, using the acromion process as a fulcrum. Sometimes a twist is necessary to further loosen the capsule, and then a push sends the head in the subcoracoid position.

The elbow can be luxated by holding the arm flat on its posterior surface on a table and then hyperextending the elbow over the edge. Sometimes a supracondylar fracture may result.

The thumb may likewise be dislocated at its metacarpophalangeal joint by simply bending it sufficiently far backward.

The hip necessitates having the pelvis firmly bound to the table by bandages, and the aid of assistants; the thigh is then hyperabducted and internally rotated. The rent in the capsule is started by the powerful hyperabduction, and the internal rotation enlarges it and sends the head out of the socket posteriorly. This dorsal luxation, by flexion and external rotation, can then be transformed into a thyroid or pubic luxation. Luxation outward of the ankle is produced by resting the lower third of the leg on a block, and allowing the foot and lower end of the fibula to project. The upper (internal) surface is then struck a powerful blow with a heavy mallet, a thick cloth intervening, and a Pott's fracture with external luxation results.

In order to avoid the occurrence of fractures of the humerus and femur, in producing luxations, it is desirable to grasp them as close to the joint as possible, and rupture the capsule by a gradually increasing pressure. Sudden, spasmodic efforts favor the production of fractures. Most useful teaching specimens can be made by first luxating a joint and then removing all except the bones and ligaments.

There is no need to discuss the preparation of specimens illustrating the ligation of arteries, amputations, resections, special operations, etc., as the methods of so doing are sufficiently evident.

How are the Preparations to be Preserved? The quality of a museum will naturally depend on the ability of the preparer, and the time and facilities at his command. Museums are not infrequently storehouses, whose contents are but rarely disturbed and only occasionally consulted.

The museum we are now discussing is to be for use, not show; it is intended to be a study museum primarily for students, to assist them in their course in applied anatomy. Secondarily, it may sometimes be consulted by graduates who are interested in special lines of work. Physicians and surgeons, not infrequently, desire to ascertain the relations of the viscera, or the topography of parts involved in operations.

Different preparations require various sorts of containers. Small specimens can be satisfactorily preserved and exhibited in glass jars. The kind of jar will, in some cases at least, be governed by the amount of money available. The cheaper

Fig. 1.—Specimen illustrative of Pott's fracture of the fibula Mounted in a rectangular glass jar.

round ones often answer the purpose sufficiently well, but where expense does not prohibit, then the imported jars with flat sides and clear glass are of course to be preferred. The covers should be easily removable and not sealed tight; the round jars are usually provided with a glass top and rubber ring. The flat jars are to be covered with a flat plate-glass cover, resting on the ground edge previously smeared with a little cosmoline. It is almost essential that all containers should be so covered as to be easily accessible so that the preparation can be removed, examined, repaired, or even replaced by a better one at will. For the majority of the specimens a flat container is preferable, and the most desirable I know of are the porcelain anatomical basins made by John Ford and Co., of the Holywood Glass Works, of Edinburgh, Scotland. These are made in several different sizes and shapes and have plate-glass covers. They have proven to be more desirable than the porcelain of domestic manufacture, and can be obtained for a very reasonable price, as, for teaching institutions, they are admitted duty free.

The porcelain lined iron tanks to be obtained from dealers in plumbers' supplies can also be used, but are not so satisfactory. If used, care must be taken to see that the rim is level so that the plate-glass cover rests even. The slightest chip in the enamel is followed by the formation of rust. Large tanks can be made of wood. They are difficult to make watertight, usually requiring coating inside with pitch or some other waterproofing substance. Lead linings or

Fig. 2.—Porcelain basins of various sizes and shapes for wet preparations. They are set in holes cut in the top of a table and rest on the flange.

paints are to be avoided, as that metal is readily attacked by the chemicals present, and is apt to deposit a white substance on the preparation, which speedily ruins it.

The porcelain basins have commonly had their glass covers sealed on by means of a paste composed of white or red lead and gold size. This was the method we first adopted and it was a complete failure. The greatest difficulty was experienced in getting the glass to adhere firmly to the porcelain. When this had been accomplished, the extremes of temperature caused the glass covers and even the porcelain basins themselves to crack. The method was so unsatisfactory that it was abandoned. Attempts to clamp the covers down on rubber gaskets by means of metal clamps were likewise unsuccessful. It was then decided to lay the cover on without sealing, and at the suggestion of Prof. Marshall the preserving liquid was overlaid with oil to prevent evaporation. The best oil for the purpose was a color-

less, heavy petroleum sold by the trade under the name oleum petrea. This was partly satisfactory, but it became discolored and its renewal was expensive.

Trial was made of a 50 per cent. aqueous solution of glycerin; this was sufficiently hygroscopic to prevent troublesome condensation on the under surface of the glass, but it also became discolored, and its renewal was too expensive, and it made the specimens (muscles and viscera) too dark.

rim of white-enamel paint. The specimens are not embedded, but sufficient plaster of Paris is placed in the basins to form a hard, flat base. On this the specimen is laid. The under surface of the specimen is to be cut away until it is level and of the desired height. Flat plates of slate can be used instead of the plaster if preferred. By this manner of preservation, the preparations can be removed at any time by displacing the lid and lifting the specimen from the alcohol.

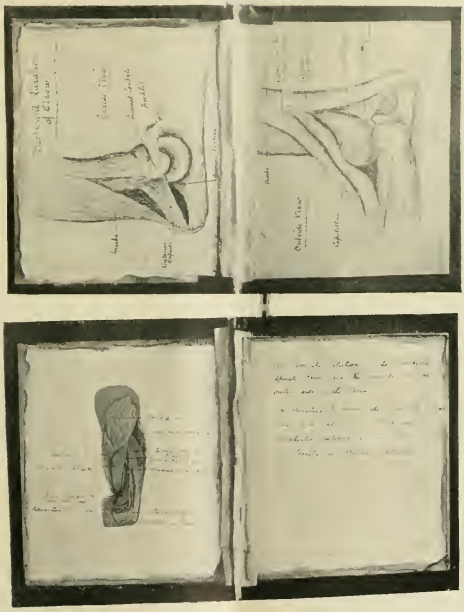

FIG. 3.—Explanatory books which accompany the specimens and are attached to the table by a chain.

Finally, commercial 95 per cent. alcohol was tried and has been found to be the most satisfactory of all.

The method now preferred is to put the specimen, as soon as it is made, in either 10 per cent. solution (approximately) of formaldehyde and allowing it to remain several days, or the No. 1 Kaiserling solution. From this it is put into pure 95 per cent. alcohol and then into the basins. The glass covers are simply laid on and, if desired, finished with a

If the latter is discolored it can be poured out and the plaster cleansed. The preparation can then be repainted or repaired, replaced in the basin, recovered with clean alcohol and the lid again laid on.

It might be objected that the specimens being so easily accessible would be disturbed by the students, but such has not been our experience.

The extent to which the alcohol becomes discolored will

depend on the character of the specimen muscular tissue and the viscera favoring it and the length of time the specimen has been in formaldehyde. The alcohol will, of course, dissolve fat out of the specimen, but when this has been removed it will remain clear. When much fat is in the solution it will form a precipitate, especially in cold weather.

Water colors are used to paint the vessels, nerves, etc. Vermilion for the arteries is quite permanent; blue for the veins is less so. Yellow for the nerves is fairly satisfactory. Zinc white is not at all stable. Green is suitable for the biliary passages, salivary ducts, etc. Owing to the easy access, repainting some of the specimens at the end of the session is not a formidable task.

An explanatory card or book is attached to each specimen.

It is recognized that these methods are not ideal, but they place it within the power of a teacher, of limited means, to obtain what so many desire, viz., a working or study museum to illustrate his course.

THE COMPARATIVE ANTISEPTIC POWER OF SALICYLIC ACID AND ITS SALTS.

By Horatio C. Wood, Jr.,
Demonstrator of Pharmacodynamics, University of Pennsylvania.

As is well known, salicylic acid is a very active germicide, distinctly superior to phenol in power. Despite this fact, and its freedom from odor, and its comparatively low toxicity, it has not come into general use as an antiseptic. One potent objection to its use as a surgical antiseptic is its comparative insolubility, requiring 308 times its weight of water to dissolve it. On the other hand, it forms with many bases salts which are freely soluble in water, and it would seem that if these salts possess an equal amount of germicidal power with the acid they would be valuable additions to our surgical disinfectants. I have, therefore, made a series of tests of the comparative strengths of salicylic acid and various of its salts.

The method employed was to mix a measured amount of an active bouillon culture with a measured quantity of a solution of the antiseptic and inoculate from this into bouillon tubes after various intervals of time. This method, while of questionable value in determining the absolute germicidal power of the antiseptic, nevertheless, as the conditions were equally favorable in either case, permits of a judgment as to the comparative strengths of two antiseptics employed in the same manner.

Salicylic acid being insoluble in water, it was necessary to add some alcohol to the solution; the amount used varied from 3 to 6 per cent., according to the concentration of the solution of the acid. That this quantity of alcohol had no influence upon the experiment was proven by tests which showed the absence of germicidal activity of a 20 per cent. solution of alcohol under the conditions, and also by using in some experiments a similar alcoholic solution of sodium salicylate instead of an aqueous solution.

Two series of studies were made, the first being carried out on a mixture of organisms obtained by exposing bouillon to the air for several days and inoculating from this into culture medium. The second series was made on the pure culture of the colon bacillus. The results can be best exhibited in tabular form:

Salicylic Acid.

Strength of solution.	*Time exposed.*	*Result.*	*Remarks.*
0.5 per cent.	1 minute.	—	Air bacteria.
0.5 "	2 "	—	"
0.5 "	5 "	—	"
0.67 "	1 "	—	"
0.67 "	2 "	—	"
Saturated aqueous.	2 "	—	"
0.33 per cent.	1 "	+	Colon bacilli.
0.33 "	5 "	+	"
0.5 "	10 "	—	"
0.5 "	5 "	—	"

Sodium Salicylate.

Strength of solution.	*Time exposed.*	*Result.*	*Remarks.*
0.67 per cent.	1 minute.	+	Air bacteria.
0.67 "	5 "	+	"
2.0 "	1 "	+	"
2.0 "	5 "	+	"
2.0 "	10 "	+	"
0.5 "	1 "	+	Colon bacilli
0.5 "	7 "	+	"
1.0 "	5 "	+	"
1.0 "	10 "	+	"

It will be seen from the above table that, although both the air bacteria and the pure culture of colon bacilli were destroyed after one minute exposure to the 0.5 per cent. solution of salicylic acid, a 2 per cent. solution of the sodium salicylate was ineffectual even after ten minutes' exposure.

As strontium salicylate has been used to some extent as an intestinal antiseptic, I made two experiments to determine whether this substance had any superior disinfectant powers over the sodium salt. In one case the colon bacillus was exposed for five minutes to a 4 per cent. solution of strontium salicylate; of the second, the culture of air bacteria was exposed for two minutes to the 4 per cent. solution of the same

salt. In both cases there was a good growth after twenty-four hours' incubation.

From the above it is evident that the neutralization of salicylic acid by either sodium or strontium very greatly diminishes its germicidal powers. This diminution in activity is far in excess of reduction in the amount of salicyl radical represented in the alkaline salts, as the sodium salicylate represents approximately 72 per cent. of salicylic acid. It would seem that the antiseptics of the aromatic series in general are much more active in acid solutions. La Place has shown that the addition of hydrochloric acid to the solution of phenol greatly increases its germicidal powers, and a single series of observations with benzoic acid and sodium benzoate which I have made indicates that the neutralization of benzoic acid gives the same results as salicylic acid.

Incidentally these results have a distinct bearing on the use of these substances as food preservatives, both the sodium benzoate and sodium salicylate being used to a certain extent as antiseptics. Although I was unable to show any marked germicidal properties with the strength of the solution of sodium salicylate employed, it was found that this substance possesses distinct antiseptic properties, a 1 per cent. solution of the salt being sufficient to prevent the development of microörganisms.

STUDIES FROM THE BACTERIOLOGICAL LABORATORY.

I. Some Observations on Three Members of the Bacterium Mucosus Capsulatus Group. II. A Note on the Effect of Toxin and Antitoxin Injections on the Phagocytosis of Diphtheria Bacilli.

By Herbert Fox, M.D.,
Volunteer Associate, William Pepper Laboratory of Clinical Medicine.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

I. Some observations on three members of the bacterium mucosus capsulatus group.

These observations were undertaken after the isolation of two strains of the Bacterium mucosus capsulatus from the lungs of very young infants who died from pneumonitis, one of which was reported by Dr. Lavenson and the writer in the Bulletin, June, 1906. The Friedländer pneumobacillus was included for comparison.

Appended is a chart of the morphological and biological characters of the three strains. (See p. 314.)

Phagocytic average of Friedländer, Lav. II, and X.

Normal average phagocytic index of the rabbits was, respectively, 1.2, 1.4, and 1.15. Immunization with twenty-four-hour serum bouillon cultures of the several strains (May 31st).

Friedländer blood with Lav. II, index 3.18. Friedländer blood with Lav. X, index 5.45. Friedländer blood with Friedländer, index 3.36.

Lav. II blood with Friedländer, index 1.9. Lav. II blood with Lav. X, index 2.9. Lav. II blood with Lav. II, index 3.8.

Lav. X blood with Friedländer, index 4.6. Lav. X blood with Lav. II, index 3.9. Lav. X blood with Lav. X, index 2.6.

Rabbits were immunized against all three cultures, so that Lav. II animal was able to withstand 10 c.c. of a twenty-four-hour serum bouillon culture into the peritoneal cavity; Lav. X and Friedländer rabbits were each able to resist 20 c.c.

No agglutinin was found in the blood of any of them, except the Friedländer for itself, reacting only in the dilution of 1 to 5.

The serum of the Lav. II rabbit contained a precipitin for the homologous filtrate to the limit of 1 to 200, but not for the filtrates of Lav. X or Friedländer. Immunization with Lav. X produced no precipitin even for the homologous filtrate. The serum of the anti-Friedländer rabbit precipitates with the filtrates of the Friedländer and Lav. II growths. The reaction was positive with the former in dilutions of 1 to 400, which limit also gave a result with Lav. II, but much less clearly. With the filtrate of Lav. X the precipitation is only feeble in the dilution of 1 to 200. These sera were drawn nine days after the last injection. The growths used for inoculation were made in serum bouillon. It will be seen that Friedländer produces a small amount of group precipitin, which body reacts to a higher limit with the filtrate of that bacterium (Lav. II) farthest from it in a biological sense.

Media 1.5+	Lav. II.	Lav. X.	Friedländer (Pepper Laboratory).
Morphology.	Gram-negative bacteria capsules in milk and animal blood, plump rod; polar staining.	Same.	Same, but no polar staining.
Agar slant.	Smooth, flat, even, regular, glistening, slimy, creamy pearl, edges wavy, stroke becoming concave, spreading only to condensed water.	Same.	Color pearl gray, not so slimy, not concave.
Agar plates.	Forty-eight hours, superficial, round, discrete, convex, entire, slimy, creamy, yellow-brown, deep, round or whetstone, brown-yellow, coarse granular	Same smaller and not so yellow	Color pearl gray and microscopically yellow, not slimy.
Glycerin.	Gas, acidity.	Very little gas, slight acidity.	No gas, neutral.
Gelatin.	Filiform along stab; no liquid, few bubbles gas, surface convex, slight umbilication, no true nail growth.	Same.	Surface more convex, but not true nail growth; all surface growths creamy yellow.
Gelatin plates.	Forty-eight hours, small, round or elliptical, entire, even, finely granular.	Same.	Same, but less yellow.
Milk.	Acidification, in forty-eight hours, coagulation, no digestion, whey pink.	Acid in twenty-four hours, no coagulation till seventy-two hours; otherwise same.	After forty-eight hours lilac which remains; no coagulation.
Potato.	Luxuriant, moist, slimy, creamy white, cheesy odor gas bubbles.	Same, but no odor.	Same, but no odor and not so luxuriant.
Bouillon	Very turbid, viscid, thick pellicle, stringy sediment, pellicle fragile.	Same.	Same, but not so luxuriant.
Peptone water.	Slightly cloudy, no pellicle, indol feebly positive.	Same. No indol.	Same. Indol faint.
Glucose agar.	Twenty-four hours, acid and gas	Same.	Same.
Lactose agar.	Twenty-four hours, acid and gas.	Same, but not so much gas.	No gas; slightly acid.
Saccharose agar.	(Lost after first subculture) twenty-four hours, acid and much gas.	Same.	Same.
Mannite agar.	Twenty-four hours, acid and gas.	Same.	Acid; very little gas.
Lactose N. Red.	Acid yellow, after four days no return of color, gas.	Acid yellow lower half, seventy-two hours partly returns, gas.	No change beyond deepening of the red.
Pathogenicity.	1 c.c. twenty-four-hour bouillon culture fatal in twenty-four hours, guinea-pigs, rabbits and mice.	1 c.c. twenty-four-hour bouillon culture fatal in twelve hours, guinea-pigs, not mice or rabbits.	1 c.c. twenty-four-hour bouillon culture fatal in 72 hours, guinea-pigs and mice, not rabbits.

On the other hand, phagocytosis with the anti-Friedländer blood is quite high with Lav. X, 5.45; while with the homologous organism it is only 3.36 and with Lav. II 3.18. The Friedländer seems to be able to produce a phagocytic as well as precipitating serum for these strains.

Lav. X, which was able to produce no precipitin, elaborated a high phagocytic power for all strains, for itself less than for the other two; viz., Lav. X, 2.6; Lav. II, 3.9; Friedländer, 4.6.

Lav. II produced relatively more phagocytic power for itself in the immune blood than for the other two bacteria or than these latter could call forth for themselves in their respective immune bloods. With the blood of Lav. II rabbit phagocytosis averaged 3.8 for the homologous organism, 2.9 for Lav. X, and 1.9 for the Friedländer. Here we notice that Lav. II was able neither to produce a precipitin nor phagocytosis for the Friedländer organism.

These biological, physiological, and chemical properties of the three strains under consideration are quite interesting, inasmuch as they show the vagaries of this group. The first two, that is, Lav. II and X, belong to the Aërogenes division, while the Friedländer is typical. That the physiology and chemistry of this latter should in any way interact with the first two is remarkable, since they are biologically distinct divisions, even though the Lav. X be nearer to the Friedländer type than is the Lav. II.

In summing up these points we see that Lav. X produces no precipitin, but its anti-blood attains a fairly high phagocytic value; Lav. II elaborates homologous precipitin, but very little increase in the phagocytic power; while Fried-

länder produces group precipitation and phagocytosis. These facts, however, offer little assistance in the determination of these species, since they are not sufficiently clear and bear no relation to the cultural characteristics. Nor does the pathenogenicity seem to clear the sky much. Inasmuch as this study was begun with the idea of examining the pneumonic processes set up by Lav. II, X, and Friedländer, the following is a *resume* of the findings in the lungs of the two babies from whom the first two were isolated, a preparation of Friedländer pneumonia in an adult, and the experimental lesions produced by all three in guinea-pigs.

When compared with the gelatinous croupous pneumonia produced by the Friedländer organism spontaneously in adults, the process produced in the lungs of the babies and experimentally bore no resemblance. The most striking thing throughout was the extensive hemorrhagic extravasation. This was marked also in all other organs. In the lung of the baby from whom Lav. II was obtained this was very pronounced and the experimental lesions were also largely hemorrhagic. The catarrhal process was seen in all the animals, but in the animal injected with Lav. X to the most marked degree. No fibrin formation was observed in any lesion. The Lav. II culture seems to have been the most virulent, since it caused death in the shortest time and gave rise to the most extensive disease. In the lungs of all the animals infected with this organism the lesion assumed the massive type and did the greatest amount of destruction. With the experimental Friedländer pneumonitis the tendency was toward the formation of miliary abscesses, or areas of catarrhal desquamation and leukocytic invasion. The pronounced feature of the Lav. X lesions was the epithelial desquamation and degeneration. The number of the mononuclear leukocytes was in direct ratio to the tendency to hemorrhagic extravasation, and in that case, *i. e.*, Lav. II, where this was at its height, they were in by far the largest number. In the lung of the animal injected with Friedländer showing the small foci of desquamation and infiltration, however, the polynuclear type predominated. When the pure desquamative changes were most prominent, as in the case of Lav. X, the two types of cells were almost equally represented. The animals were all injected into the abdominal cavity with twenty-four hours' bouillon cultures. The distribution of the bacteria is not very clear, and it is difficult to say where they lie by preference. It seems, however, that they are most abundant wherever the hemorrhagic extravasation or leukocytic infiltration is greatest. They are frequently seen in the septa and are not abundant where the pure desquamation predominates. Such a distribution, of course, might be expected, since the bacteria were carried to the lungs by the blood stream,

II. A NOTE ON THE EFFECT OF TOXIN AND ANTITOXIN INJECTIONS ON THE PHAGOCYTOSIS OF DIPHTHERIA BACILLI.

This report concerns the results of one experiment on the effects of variously combined injections of diphtheria bacilli, toxin and antitoxin (commercial) upon the phagocytic power of rabbits' blood. The toxin was the filtrate of a four weeks' old culture of the bacterium, and was fatal for guinea-pigs in doses of 1.5 c.c. in forty-eight hours. The results set down in the table are phagocytic averages and not opsonic indices.

Rabbits were subcutaneously injected (in different localities when more than one injection was made) in quick succession and the first observation was made after the lapse of four hours. Both blood and serum were drawn, the former being defibrinated by sodium citrate solution. In preparing the emulsion of corpuscles the same amount of blood was drawn in order to have the number of leukocytes approximately the same. The emulsion of the bacilli was made in normal salt solution and washed twice. In order that the results might be comparable, the number of bacilli in the emulsion at the three tests was counted, and the figures in the table are on the common basis of the lowest count. In setting the tests 0.1 c.c. of the various emulsions and sera was pipetted into tubes and the whole made up to 0.6 c.c. with normal salt solution. The smears were made after the tubes had been one hour at 37° C.

The first thing which strikes one's attention in looking over the table is the marked decrease in the average phagocytosis at the test made three days after the injection, the negative phase of opsonification. Even in the blood of the animal which had received the antitoxin alone is this true, but to a relatively less degree than in the others.

The immediate (after four hours) effect of the injections seems to be negligible except in the case where the toxin was injected alone. Here the average rose from 3.6 to 4.5, a rise of 0.9. This may have been due to a sudden stimulation of the leukocytes "in vivo" and carried on when the blood was shed; the same thing was not observed with the normal corpuscles and "B" serum, nor in the blood of rabbit "C," which received both bacilli and toxin, probably because the organisms anchored the opsonin stimulated to action by the toxin. The marked drop in phagocytosis after seventy-two hours in this "B" rabbit's blood may be an excessive negative phase due to the presence of overwhelming poison. (This animal and Rabbit "A" died in ten days, preventing the extension of the experiment to five tests as primarily intended.) The lower average with normal leukocytes may be because they had not been stimulated by a virus.

From the reactions of the blood of Rabbits "D" and "E"

it would seem probable that the injection of antitoxin into animals has little to do with phagocytosis, since the averages of these bloods throughout permit of comparison with that of "A." which received the bacilli only.

When we look at the reactions which occurred after eight days we notice an increase over those which were found in the previous test, except with "C" serum and normal blood, a low figure which I am unable to explain. I am also unable to explain the marked rise of the phagocytic average with "C" serum and corpuscles.

The last averages of the rabbit receiving toxin are relatively lower than the averages of the blood of the animals receiving bacteria, either alone or in combination, and lower relatively than the animal receiving antitoxin alone. It would seem that the toxin depresses the action of the opsonins when acting "in vivo," that is, the phase of stimulation is succeeded by a lasting depressing or negative stage.

The results of this experiment are offered with the full realization that they, of themselves, have little value, but they may supplement the work of some other observer or suggest a line of work to him. They were suggested by Prof. Stengel, and it is with his sanction that I offer them.

PHAGOCYTOSIS OF DIPHTHERIA BACILLI.

		4 hours.	72 hours.	8 days.
Normal serum and leukocytes (simultaneously with below) + Bact. diphtheria		1.7	1.2	1.6
A. Injection of washed diphtheria bacilli, 1 c.c. emulsion.	"A" blood and serum + Bact. diphtheria	2.0	1.0	2.3
Before injection 2	"A" serum + normal leuk. + Bact. diphtheria	2.2	0.8	1.7
B. Injection of toxin alone, 1 c.c.	"B" serum and leuk. + Bact. diphtheria	4.5	1.3	1.8
Before injection 3.6	"B" serum + normal leuk. + Bact. diphtheria	2.4	1.0	1.1
C. Injection washed diphtheria bacilli emulsion 1 c.c. and toxin 1 c.c.	"C" serum and leuk. + Bact. diphtheria	3.5	0.5	4.2
Before injection 3.9	"C" serum + normal leuk. + Bact. diphtheria	4.0	1.7	1.0
D. Injection washed diphtheria bacilli emulsion 1 c.c. and antitoxin 250 units	"D" serum and leuk. + Bact. diphtheria	4.6	1.6	3.8
Before injection 4.8	"D" serum + normal leuk. + Bact. diphtheria	5.0	2.0	3.3
E. Injection of antitoxin 250 units	"E" serum and leuk. + Bact. diphtheria	3.5	1.3	2.5
Before injection 3	"E" serum + normal leuk. + Bact. diphtheria	3.4	1.3	2.5

THE EFFECT OF LIGHT ON THE DEVELOPMENT AND STAINING OF OVA IN EOSIN SOLUTIONS.

By L. P. Shippen, Med. 1907.

It has been shown by a number of investigators, especially by Ledoux-Lebard, v. Tappeiner and Jodlbauer, Straub, and Edlefsen that cells and certain ferments upon the addition of fluorescent stains are injured much more readily if kept in the light than if placed in the dark. Such investigations were carried on mainly with certain protozoa and ciliated epithelium, and it was of interest to examine the influence of such conditions upon eggs which were capable of development in order to determine how other functions of cell life, such as embryonic development, were affected by eosin under the influence of light and darkness.

Several varieties of eggs were used in these experiments, because it was possible that there existed a difference in resistance in the various ova; furthermore eggs in different stages of development were examined in order to determine if the power of resistance varied according to the stage of embryonic development. Besides observations were made on the staining of cells with eosin, and it was found that in

living motile organisms certain parts could be stained by eosin.

These experiments were carried out during the summer of 1905 in the Marine Biological Laboratory at Wood's Hole, Mass., under the direction of Dr. Leo Loeb.

The eggs and sperm used were obtained from Asterias, Chætopterus, and Arbacia, and solutions of eosin in ordinary sea-water in strengths of 1 to 1000, 1 to 10,000, and 1 to 50,000 were employed in the experiments. The eggs and sperm, or in some cases the gastrulæ were dropped by means of a pipette into two sets of finger bowls containing the above solutions, and one set of finger bowls was then placed in places protected from the light, while the remaining set was placed near a window so that diffuse light, but no sunlight, should fall upon it. In addition eggs were fertilized in ordinary sea-water, and placed under similar conditions in order to act as controls.

The following is a short resume of some of the experiments thus performed:

Experiment 1.—Fifty drops of eggs and ten drops of sperm obtained from Asterias were placed in eosin solutions of 1 to 10,000 and 1 to 50,000 strengths, and into controls of sea-water; 50 c.c. were used in each solution.

After six hours had elapsed it was noticed that in the controls, both in the light and in the dark, nearly all the eggs had developed to the thirty-two or sixty-four cell stages. In both the 1 to 50,000 eosin solutions fewer eggs had developed and in the 1 to 10,000 eosin solutions the vast majority of eggs showed no sign of cleavage whatever. But those eggs that had developed seemed as far advanced in the eosin solutions as in the controls, and no difference was observed between the eggs kept in the dark and those kept in the light.

After twenty-four hours the eggs in both the controls had developed into gastrulæ which were seen in large numbers and the eggs kept in the 1 to 50,000 eosin solution in the dark had likewise reached the gastrulæ stage and seemed as numerous as in the controls; but the eggs kept in the 1 to 50,000 eosin solution in the light had for the most part failed to develop, and only a few gastrulæ were seen. In the 1 to 10,000 eosin solution kept in the dark only one or two gastrulæ could be discovered, while in the solution of the same strength kept in the light none whatever were found.

Experiment 2.—Gastrulæ, twenty-four hours after fertilization were placed in eosin solutions of 1 to 10,000 and 1 to 50,000 strengths. 25 c.c. were used in each solution, and the experiment was conducted in the manner already outlined.

After six hours had passed many of the gastrulæ in the 1 to 10,000 eosin solution kept in the light were seen to turn violently on their axes and to remain in the centre of the microscopic field. While in the other solutions and in the controls all the gastrulæ moved freely and rapidly in every direction.

At the expiration of twenty-two hours the organisms in the 1 to 50,000 eosin solution in the dark were as motile and as well developed as those in the controls; while the organisms in the 1 to 50,000 eosin solution in the light seemed less normal in development, though no staining reaction was noted. But in the 1 to 10,000 solution in the light many motile organisms were distinctly stained, fewer were motile, and many turned only on their axes. In the 1 to 10,000 solution in the dark the conditions were much better. Only a few of the organisms were stained, or turned on their own axes, while many were freely motile.

After twenty-eight hours a marked difference was noted between the organisms kept in the 1 to 10,000 eosin solution in the light, and those in the other solutions. They were much shorter, contracted in the centre and were deeply stained pink, but were highly motile, while in the 1 to 10,000 solution kept in the dark, the organisms were but little if at all stained, and were better developed. In the 1 to 50,000 solution in the light the organisms were shorter than those kept in the solution of the same strength in the dark, and were colored a brownish tint. The motility of the organism in all of the solutions was very good.

After thirty hours the controls contained many normal, motile organisms, while those in the 1 to 50,000 solution kept in the dark were contracted and shorter and this difference was even more marked in the organisms in the 1 to 50,000 solution in the light. In the 1 to 10,000 eosin solution kept in the light all the organisms were stained and dead, and many were shrivelled and irregular. While in the solution of the same strength in the dark many of the organisms were also dead, stained and shrivelled, but a few fairly normal motile ones were also seen, and in these no staining reaction was noted.

Experiment 3.—Eggs of Chætopterus were fertilized and half an hour later, when some eggs were in the two-cell stage, fifty drops of the eggs were placed in 25 c.c. of 1 to 1000, 1 to 10,000, and 1 to 50,000 eosin solutions.

After six hours the motility of the organisms was found to be much greater in the solutions kept in the dark, and the weaker the solution the greater was the motility of the organisms. In the 1 to 50,000 and 1 to 10,000 solutions kept in the light the organisms had merely slight ciliary motion, while the organisms in the 1 to 1000 solution in the light possessed no motility at all.

After thirty hours sunlight fell on the solutions kept in the light for a period of two or three hours, and in all these solutions, including the control, the organisms were agglutinated and dead; but in the dark agglutination and death were complete only in the 1 to 1000 solution. In the 1 to 10,000

solution a few, free, swimming organisms were seen, while in the 1 to 50,000 solution and in the control many organisms were motile, and only a trace of agglutination was observed.

Experiment 4.—Eggs of a sea-urchin were fertilized and forty-five minutes later seventy-five drops were placed into each of 25 c.c. of 1 to 1000, 1 to 10,000, and 1 to 50,000 eosin solutions.

No especial difference was observed between the organisms kept in the light and those kept in the dark until about thirty hours had elapsed, when the motility seemed worse in the light 1 to 50,000 solution than in the 1 to 50,000 solution in the dark.

After two days and six hours the motility and development of the organisms in the 1 to 10,000 and 1 to 50,000 solutions kept in the dark were markedly better than in solutions of equal strength kept in the light; but between the organisms in the two 1 to 1000 solutions no difference was observed.

After three days the gastrulæ in the 1 to 1000 solution in the light were all dead and stained, while in the solution of the same strength kept in the dark the gastrulæ were practically all motile and unstained. No plutei were seen in either solution. In the 1 to 10,000 solution in the light the gastrulæ were slightly motile, about 10 per cent. were dead and stained, and no plutei were seen; but in the solution of the same strength in the dark over 50 per cent. were actively motile plutei, while the remainder consisted of motile gastrulæ. The dead were so few in number as to be difficult to find. In the 1 to 50,000 light solution about 3 per cent. or 4 per cent. were slowly motile plutei, and the remainder consisted of slowly motile gastrulæ or deformed plutei. In the dark solution of the same strength there were over 50 per cent. of motile plutei, too active to be counted accurately, while the remainder consisted of gastrulæ or deformed plutei, more motile than those kept in the 1 to 50,000 light solution. The controls contained practically only actively motile plutei, and staining was seen only in dead organisms in the eosin solutions kept in the light.

These and a number of similar experiments would seem to indicate that eosin in strengths of 1 to 50,000, 1 to 10,000, and 1 to 1000 has an inhibiting effect upon the development of ova both in light and in darkness, but that this effect is much more readily produced under the influence of light.

The growth of the organisms in the eosin solutions kept in the light was both irregular and retarded and the effect was more marked in the stronger solutions. In the dark this result was much less distinct, and at times in the weakest solution of 1 to 50,000 strength it was even hardly noticeable. Also cessation of motility and death of the organisms were found to occur earlier in solutions under the influence of light than in those placed in the dark. And here too the 1 to 50,000 solution in the dark produced but very little effect upon the motility and length of life of the organisms.

In addition the same results were obtained when the ova of the star-fish were allowed to develop into gastrulæ before being placed in the various solutions.

The eggs of the sea-urchin were found to be much more resistant to the action of eosin both in light and dark than were the eggs of the star-fish or chætopterus. But this may have been due to some unknown condition acting during the summer of 1905. However, the final result was even more marked than in the case of the other ova.

In regard to the staining reactions the experiments performed were not sufficiently definite to enable any accurate conclusions to be drawn, but in some further observations made by Dr. Loeb in the summer of 1906 it was found that living as well as dead blastulæ and gastrulæ stain in part with eosin.

This is in apparent opposition to the fact that eosin is not an intravitam stain. But when the stained motile organisms were examined with a higher power it was observed that the eosin did not affect the cells which formed the layer of the blastula proper, nor the ectoderm or endoderm of the gastrulæ, but that the eosin did stain the cells or parts of cells which lay beneath the outside cellular layer. Now these stained cells were in all probability not healthy, but either dead or dying. For they seemed to be partially disintegrated, and furthermore the cells which were certainly healthy, namely, those which formed the blastula proper, and those in the ectoderm and endoderm of the gastrulæ did not take up the eosin at all.

If, on the other hand, intravitam stains were used, such as neutral red or in lesser degree methylene blue, it was found that the outer layer of cells of the blastula and the ectoderm and endoderm of the gastrula took up the stain.

It is possible for blastulæ and gastrulæ to discard cells into their internal cavities, as well as to cast them off on the outside. The blastulæ and gastrulæ can show ciliary movements inside of their membranes. Under these conditions it was found that cells showing ciliary motion were not stained by the eosin, but that the cast off cells did take up the stain. If, on the other hand, such larvæ were stained with neutral red the reverse condition was true.

Thus it is seen that staining with eosin enables us to recognize the dead and dying cells in living organisms.

In agreement with this observation that dead cells in gastrulæ stain with eosin is the fact that those larvæ which were farthest and most normally developed and which possessed the best motility showed the least stain. For the most part the smaller and more irregular ones were those which took up the eosin stain.

It is a question of great interest, how it is possible for

eosin to stain dead cells which are entirely surrounded by living ones. Of course it might be possible that cells take up eosin in the outer layer just before being cast off, but then some cells in the outer layer would also be stained, and this condition was never observed. Therefore it is more likely that eosin penetrates the outer layer and stains the dead cells inside the cavity.

If larvæ develop still further to bipennariæ it is not possible to observe any taking up of stain in cells in the body cavity. On the other hand, it is not infrequently possible to see particles stained by eosin inside the intestinal tract of bipennariæ, or inside the endodermic cavity of stages intermediate between gastrulæ and bipennariæ. But, here we have in all probability to deal with a different process. Bipennariæ very readily take up dead particles stained with eosin, or even living protozoa that include eosin stained particles in their cell bodies, and the eosin stained contents of these are merely taken up as foodstuffs.

Summary.—In summary the following facts were noted:

1. Eosin inhibits the development of ova and injures the motility of gastrulæ and blastulæ, and in time kills them.

2. Light has an additional injurious effect upon the development of ova and the motility of larvæ in eosin solutions, and shortens the life of the blastulæ and gastrulæ.

3. Certain parts of living organisms can be stained by eosin. It is very probable that the cells of living organisms which take up eosin are dead or dying. Eosin enables us therefore to recognize dead or dying cells in living organisms. It is furthermore of interest that cells which take up eosin may be entirely surrounded by a layer of living cells.

BOOK REVIEWS.

A Manual of Medical Treatment or Clinical Therapeutics. By I. Burney Yeo, M.D., F.R.C.P., Emeritus Professor of Medicine, King's College, London; Consulting Physician to King's College Hospital; Hon. Fellow of King's College; Formerly Professor of Principles and Practice of Medicine and of Clinical Therapeutics in King's College, and Examiner in Medicine at the Royal College of Physicians; author of *Food in Health and Disease*, etc. Revised edition, with Formulæ Adapted to Standard of Strength of Preparations Employed in America, by Oscar Oldberg, Ph.D., Dean of the School of Pharmacy of Northwestern University; Member of the Committee of Revision of the Pharmacopœia of the United States. Fourteenth edition. Twenty-second thousand. Vols. I and II. Chicago: W. T. Keener & Co., 1906.

This manual is really a study of therapeutics from the side of the disease rather than from the study of the drug or remedy used, an especial effort being made to emphasize the relation of the remedy to the indications as shown in the etiology, pathology, and symptomatology of the disease. There have been fourteen editions of the work since 1893, with three revisions, all of which speak well for its popularity. The work is abreast of the times and is remarkably free from new and imperfectly tested methods, possibly a little too conservative in this regard. Among the additions to this edition are articles on hay fever, paralysis agitans, cerebral tumors, erysipelas, cerebrospinal fever, rickets, scurvy, and purpura. The manual has been published in two volumes of about 700 pages each. The diseases are taken up and discussed by systems. This fact, together with an unusually complete index, makes reference to subjects easy and simple. The description of each disease with the discussions on etiology and symptomatology are brief, but full enough to point out the proper indications for treatment. The strength and nomenclature of the medicinal preparations are based on the British Pharmacopœia, and in the first volume there is a table in which the strengths of the preparations are compared with those of the recent revision of the United States Pharmacopœia. At the end of each section are appended prescriptions in addition to those given in the text. Mineral waters are advocated in preference to laxatives or purgative drugs for increasing the activity of the intestinal tract. The climatic treatment of tuberculosis is dwelt on at some length, and concludes with a list of sanatoria located in the Isles and on the Continent. Creosote is given the prominent place among drugs used in tuberculous conditions. Condurango is suggested in gastric carcinoma for relief of pain, improvement of digestion, and increasing pancreatic and hepatic secretions. Surgical measures in various conditions are given their proper place. The author discountenances the routine treatment of typhoid fever by baths, preferring the use of packs, giving in addition phenacetin in combination with quinine, in cases where the temperature is very high. The work, as a whole, is well written, systematic, and up to date, and in many ways a valuable contribution to the study of therapeutics and medicine.

F. H. K.

Physiology of the Nervous System. By J. P. Morat, of the University of Lyons. Authorized English edition translated and edited by H. W. Syers, M.A., M.D. (Cantab.), Physician to the Great Northern Central Hospital. 263 illustrations (66 in colors). Chicago: W. T. Keener & Co., 1906.

The work of Morat on the physiology of the nervous system is an important addition to the literature of that subject. The book has been translated by Syers and, in consequence, is brought to the attention of a great number of readers in this country and in England. The work is

of considerable value, both to the special student in this field and to the specialist in nervous diseases.

It is indeed pleasing to read this book, for it differs greatly from others upon this subject, which are simply repetitions of what already has been compiled by other authors, in that it possesses individuality as well as originality. Instead of being cumbersome and teeming with data the book presents the essential fundamental facts in a logical sequence, discusses mooted problems with brevity and clearness, and, above all, gives the reader a broad conception of the subject as a whole. Every page gives evidence of the fact that years of careful thought preceded the writing of the first line. Equally evident is the fact that the translator has been very accurate in his work and he gives us a very readable book.

The first chapter is devoted to a consideration of the neuron or nervous element. Invariably, the author takes a general view, and his broad reasoning helps the reader materially in obtaining a clear understanding of the subject. Thus, he maintains, in considering the laws governing the nerve cells, that "they are not only applicable to elements composing the nervous system, but to every cell element." This fact is overlooked by many investigators in this subject, and leads frequently to narrow and biased conclusions. However, the author recognizes the differentiation of the neuron and assigns to it a special function, namely, the directing of the energies developed in other cells. In other words, the neuron simply regulates the activities of the other cells in the body and causes their co-operation.

The chapter also contains a description of the apparatus used for studying the functions of the nervous system. The apparatus is clearly and concisely described, and this portion of the book will be of great interest to the clinician who has not had a training in the experimental side of this subject.

The succeeding chapter on nerve energies is given over, in a large part, to the study of electrotonus; but other subjects, such as nerve fatigue and nerve poisons, are also considered. In a discussion of the problem as to whether "an impulse, travelling from the receptive to the distributive pole of the neuron, passing through the body, undergoes a modification in it," he decides, contrary to the belief of many authorities, that no such modification occurs.

The succeeding chapters are all introduced by a broad and philosophic discussion of the subject before the details are presented. This often leads the reader, because of an unpreparedness, to doubt many of the assertions. He divides the nervous system into two portions, the sensory and motor, but, observing the subject from another point of view, he divides it into "two great systematizations, founded on another opposition, that which exists between the conscious and unconscious nature of certain acts or functions which it performs." In other words, the writer, at one time studies the nervous system from the point of view of sensation and motion, and, at another time, from the relation of the conscious and unconscious. For a time, the classification leads to confusion in understanding many facts at hand, but becomes clear when these points are further elaborated. In considering this aspect of the subject, he does not recognize an absolute opposition between sensation and motion, or consciousness and unconsciousness, but that there are intermediary gradations so numerous that conditions at times apparently opposite may, at other times hardly be differentiated. The varying degrees of complexity in sensation and motion lead him to consider three forms. First, the reflexes which demonstrate the transformation of sensory into motor excitation; secondly, inhibition, which is described as preventing immediate effect of sensory excitation and suspends or postpones the motor effect; lastly, he speaks of an "inverse bond existing between movement and sensation which permits them to maintain themselves mutually in the organism, in an automatic fashion, thus preserving the impulse in its interior, by a genuine circulation comparable to that of matter and of energy." A discussion of this classification would be so involved as to occupy too much space, but the views which follow are both interesting and instructive.

Under the head of superior systematizations, he refers to the functions of the nervous matter above the pons. He here discusses such subjects as equilibration and the emotions. In referring to pain he describes it as the "internal revelation of functional disorder." "Pain appears as the consequence of every excitation, which, by its intensity or its abnormal repetition, transgresses the conditions requisite for the maintenance of the functions in good order." He further adds that there is no organ of special pain sense nor are there special conductors of pain. The book concludes with a study of the special senses, language and ideation.

All in all, the book is of a high degree of excellence and will appeal to every thoughtful reader. E. L.

The American Illustrated Medical Dictionary. A New and Complete Dictionary of the Terms Used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry, and Kindred Branches, with their Pronunciation, Derivation, and Definition; Including much Collateral Information of an Encyclopedic Character. By W. A. Newman Dorland, A.M., M.D., Assistant Obstetrician to the University of Pennsylvania Hospital; Editor of *American Pocket Medical Dictionary;* Fellow of American Academy of Medicine. Together with New and Elaborate Tables of Arteries, Muscles, Nerves, Veins, etc.; of Bacilli, Bacteria, Diplococci, Micrococci, Streptococci, Ptomaines and Leucomaines, Weights and Measures, Eponymic Tables of Diseases, Operations, Signs and Symptoms, Stains, Tests, Methods of Treatment, etc. Fourth edition, revised and enlarged. Philadelphia and London: W. B. Saunders Co., 1906.

The foregoing enumeration, taken from the title-page of the work, practically explains its scope. The author has endeavored to compile a dictionary sufficiently exhaustive for practical use without making the volume unduly cumbersome. In this he has, in a very large measure, succeeded. As has already been stated the scope of the work is not limited to medicine alone, but contains such matter pertaining to kindred sciences as a physician of liberal education would be likely to require. Of course, a work of such amplitude is apt to contain some oversights and omissions. We mention the following, with the suggestion that they be included in future editions as omissions which have come to our notice,

rather for the sake of completeness than because they seriously militate against the value of the work as a book of reference: Eustace Smith's sign of enlarged bronchial glands, McCarthy's or the supraorbital reflex, Adams-Stokes disease, the auriculoventricular bundle of His, and Traube's murmur.

We have no hesitancy, however, in recommending the dictionary as a most useful book for the physician to keep on his desk. G. W. N.

Infection, Immunity and Serum Therapy in Relation to the Infectious Diseases which Attack Man; with Considerations of the Allied Subjects of Agglutination, Precipitation, Hemolysis, etc. By H. T. Ricketts, M.D., Instructor in Pathology, University of Chicago. American Medical Association Press; 1906.

The substance of the work before us appeared in a series of special articles in the *Journal of the American Medical Association* during 1905, which received much favorable comment. The author has now published these articles in book form, revised, and with additions bringing them up-to-date.

The subjects embraced in the title have for the past ten years been fields for especially fruitful research, and every day has added new data concerning the processes involved. The brilliant work of Metchnikoff and Bordet at the Pasteur Institute, and the no less brilliant researches of Ehrlich in Germany, which gave birth to his "side-chain" theory, stimulated workers in all parts of the world, the result being that a veritable torrent of facts has poured forth in the current literature, for the description of which a practically new vocabulary has been invented. The average medical man who wishes to keep in touch with new discoveries has been hopelessly puzzled and even the specialist in laboratory work has had difficulty in keeping pace with the advances reported.

The book of Dr. Ricketts has therefore been welcome to all classes, giving, as it does, in compact form a review of the enormous mass of literature, the originals of which are widely scattered in journals printed in all languages. The task has been colossal, and has been well performed.

The arrangement of the book is such that it can be read understandingly by the student, or the physician not versed in special research, beginning with the fundamental principles and working up historically to the more complex phenomena and their explanations. It is in two parts, the first being given up to the general discussion of the facts and theories involved, while the second takes up the special consideration of the infectious diseases. An appendix treats of Welch's theory, and the Aggressins of Bail.

The book is a valuable and reliable summary of the present state of our knowledge of the subjects embraced in the title. It is thoroughly up-to-date, giving the latest data on subjects so new as the Opsonins of Wright and Douglass, and the occurrence of the Spirocheta pallida in syphilis. The author possesses in a marked degree the valuable talent of abstracting the meat of a subject and presenting it to his readers in an intellectually palatable condition.

The printing is in clear type on good paper. The index is good and the sub-headings of the chapters are given in heavy type on the margins, a plan which greatly facilitates reference to any subject. M. P. R.

Manual of Anatomy: Systematic and Practical, Including Embryology. By T. M. Buchanan, M.A., M.D., C.M., F.F.P.S. Glasgow, Professor of Anatomy in Anderson's College, Glasgow; Examiner in Anatomy for the triple qualification in the Scottish licensing bodies; Examiner in Anatomy and Physiology for the Dental Diploma, and Examiner in Anatomy (human and comparative) for the Fellowship of the Faculty of Physicians and Surgeons of Glasgow; Reëxaminer in Anatomy to the University of Glasgow; formerly Senior Demonstrator of Anatomy in the University of Glasgow, etc. Vol. I, Osteology; Upper Limb; Lower Limb. With 268 illustrations, mostly original and in colors. Chicago: W. T. Keener & Co., 1906.

This pleasant production is an output of the British School, which is doing such good work along anatomical lines. It is regional in arrangement, beginning with the skeleton, to which the first part is allotted, and continuing with descriptions of the upper and lower extremities, with which the present volume ends. The style is clear and simple, marked by avoidance of ultra-technical terms, the writer evidently being aware of the difficulties with terminology under which the medical neophyte labors. The illustrations are copious, in the main original and in character leaning toward the diagrammatic. At times they are crude and throughout are characterized by flatness and absence of perspective and artistic beauty. Due attention is bestowed on the minute anatomy and development of the parts treated, and the volume is concluded with a good index.

No pretensions are made to approach the standard of the elaborate and monumental works of the Fathers, and the character of the book can best be described by saying that it will make an excellent and readable volume wherewith either the graduate or undergraduate student may review and refresh his knowledge of anatomy. In this capacity it should assume high rank. G. F.

A Treatise on Orthopedic Surgery. By Royal Whitman, M.D. Third edition, revised and enlarged. 554 illustrations. Philadelphia and New York: Lea Brothers & Co., 1907.

Four years have elapsed since the second edition was issued. The present or third edition has been slightly enlarged by the addition of 23 pages and 47 illustrations, besides the substitution of new for some of the original cuts.

The general character and size of the work remains but little altered. The text has been revised and in some places rewritten. Less space is devoted to forcible correction of

the deformity in Pott's disease; short sections are devoted to relaxation of pelvic joints following pregnancy and some other conditions; also to cervical ribs and scapular crepitus. Referring to Bier's treatment it is stated that the treatment of infectious processes of joints and other tissues by passive congestion has now come into general use.

About half a page is devoted to the consideration of rheumatism and gout. Rydygier's method of excision of the hip, Hoffa's operation for paralysis of the deltoid by transplanting the trapezius, and Goldthwait's of transplantation of the sartorius are also described. Among the new illustrations are two of tuberculous disease of the shoulder and wrist; one illustrating bilateral congenital pronation of the forearms; one each of osteitis deformans and axillary abduction (Werndorff) for congenital luxation of the hip. There are two new cuts each for fracture of the neck of the femur, paralysis of the deltoid and transplantation of the trapezius, and of the method of manipulating flat feet. The volume is gotten up in the same excellent typography and style as have characterized the previous editions. While it cannot compare in completeness nor thoroughness with some of the modern German works on the same subject, it still presents, in a compact form, the modern methods of treatment of orthopedic affections. G. G. D.

The Ear and its Diseases. A Text-book for Students and Physicians. By Seth Scott Bishop, B.S., M.D., LL.D., Honorary President of the Faculty and Professor in the Post-Graduate School and Hospital of Chicago; Surgeon to the Post-Graduate Hospital and to the Illinois Hospital, etc. Illustrated with 27 colored lithographs and 200 additional illustrations. Royal octavo, 440 pages. Philadelphia: F. A. Davis Co.

The subject matter of this clearly written and well-printed volume is based upon a practice extending over twenty-five years. Such a long experience enables the writer to speak authoritatively about many of the rarer diseases, and this forms one of the most valuable features of the book. The author has kept closely in touch with the progress of otology, and the work is entirely modern in tone. The illustrations are numerous, new, and for the most part good, and the operative technique, especially for opening the mastoid and for intracranial complications, is as complete as the space allows. Upon several subjects one may find himself at variance with the author, as for instance when he recommends, in certain forms of chronic non-suppurative otitis media, the use of inflation through the Eustachian tube by means of a compressed air apparatus giving a pressure of sixty pounds. For the most part the teaching is safe and practical, and the book is complete without being exhaustive.

W. G. B. H.

Genito-urinary Diseases and Syphilis. By Henry H. Morton, M.D., Clinical Professor of Genito-urinary Diseases in the Long Island College Hospital; Genito-urinary Surgeon to the Long Island and Kings County Hospitals, and the Polhemus Memorial Clinic. Illustrated with 158 half-tone and photo-engravings and 7 full-page colored plates. Second edition, revised and enlarged. Royal octavo, 500 pages. Philadelphia: F. A. Davis Co.

Dr. Morton has put before students and practitioners a most valuable book. It is concise and the conciseness is one of its best features. It is as up-to-date as is possible in the present rapid progression of all branches of medicine.

It is a pleasure to see Janet's irrigation given the place and attention it deserves, and Dr. Morton, like all men who have tried total irrigation, sees the advantages and disadvantages, which are fairly set forth.

As a text-book it is the best we have seen for some time and as a reference book it deserves a place in any man's library.

E. H. S.

Essentials of Medical Electricity. By Edward Reginald Morton. London: Henry Kimpton; Chicago: W. A. Keener & Co.

This book is a compendium of the various ways in which electricity may be used as a means of diagnosticating and treating disease. The author has been successful in condensing much knowledge into a small compass, so that the result is not, by any means, simply a primer. The style is clear and concise and the tone conservative. Numerous illustrations assist in making clear points difficult of description. The *x*-rays and the various treatments by light are not considered as properly belonging to electrotherapeutics and therefore are not discussed. For the methods of using electricity in gynecology the reader is referred to a work on that subject.

C. D. C.

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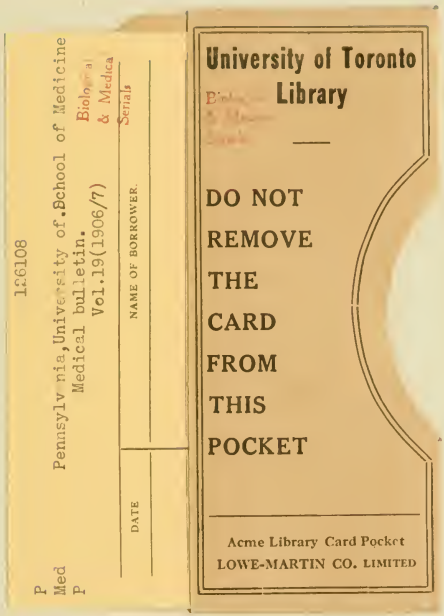
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